Archives of Dermatology and Syphilology

VOLUME 21 MAY, 1930 NUMBER 5

CUTANEOUS MANIFESTATIONS OF HEREDITY*

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For many years, heredity has been recognized as an important factor in all branches of medicine, but its mode of operation was never clearly defined, and indeed could not be understood until the clue given by Mendel was followed up. With this guide, it has been possible to begin to unravel the mystery, but progress is slow for several reasons: 1. It is impossible to control the material. It might be illuminating if one could mate two persons suffering from the same disease, and study the progeny, but instead one has to be content with taking the matings as one finds them. 2. The generations are so long and the records so imperfect that such statistics as are available are fragmentary and subject to error. 3. The stock is so thoroughly mongrel that it is almost impossible to say what traits may remain latent for many years, unable to make themselves manifest until a chance mating produces an individual homozygous for that trait. The difficulties are great enough when the condition under discussion is governed by a single mendelian factor, but they are much greater when, as is usually the case, the condition is produced by the combination of several mendelian factors, and still greater when some stimulus, external or internal, is necessary to convert the hereditary possibility into an objective reality.

A great deal of the confusion arises from the impulse to consider any disease as a single thing, an entity, to be inherited as a unit. This assumption may be valid for certain cutaneous peculiarities, but it is not valid for the great mass of disease conditions. I shall consider first this class of cutaneous peculiarities, as they are the simplest and most easily understood in their mode of inheritance. Albinism is the simplest of all. Albinism is a complete lack of pigment in skin, hair and iris; its victim has no power of producing pigment, and he cannot transmit to his offspring what he himself lacks. The condition is a mendelian recessive, using that word in its broad sense, and without

* Submitted for publication, Oct. 19, 1929.

* Read at the Fifty-Second Annual Meeting of the Dermatological Association, San Francisco and Del Monte, July 1, 1929.

choosing between the dominant and recessive theory on the one hand and the presence and absence theory on the other. When two albinos mate, the offspring are all albino, because neither parent is able to transmit the power of producing pigment. If an albino mates with a normally pigmented person, in whose ancestry there are no albinos, all the offspring will be normally pigmented; all the germ cells of the normal parent carry the power to produce pigment. Similarly, the germ cells of a blue-eyed person carry the power to produce the blue pigment of the iris, but do not carry the power to produce any brown pigment in the iris; therefore, the offspring of two blue-eyed people are always blue-eyed. A black-eyed person has blue pigment in the iris, but the blue is overlaid and concealed by black pigment. All his germ cells carry the power to produce both black and blue pigment in the iris, and the offspring of a black-eyed pair are black-eyed, as the black color conceals the blue. But with brown-eyed people, the conditions are different. The iris still has blue pigment, and all the germ cells carry the power to produce blue iris pigment. The blue in the iris, however, is overlaid by something less than the full amount of black pigment; some of the germ cells from such a person will carry the power to produce black pigment in the iris, while others will lack this power. When brown-eyed people mate, therefore, the color of the eyes of the offspring is a matter of chance. If the two germ cells both carry the power to produce black eye pigment, the child will have black eyes, if one carries the black factor while the other does not, the child will have brown eyes, while if neither germ cell carries the black factor, the child will have blue eyes, because all germ cells, except those from albinos or with albino ancestry, carry the power of producing blue eye pigment. For the sake of simplicity, it is here assumed that blue pigment and black pigment are each carried by a single factor, but it is probable that several factors are involved, particularly in the case of black pigment. This occurrence of blue eyes among the offspring of brown-eyed parents is a typical example of the behavior of recessive qualities, but it has proved a stumbling block to those who are not familiar with its mechanism. It is hard to convince the ordinary person that a character which has not been observed in the ancestry for generations is definitely inherited in accordance with known laws. The occasional birth of a red calf in a herd of black and white Holstein cattle, pure-bred for many generations, is another example of the same sort. Red is recessive to black in Holstein cattle, which originally were either red or black; a chance mating of two cattle, both black, but heterozygous, will produce an occasional red calf. The mode of inheritance in these cases is fairly well understood because the manifestations are common, easily recognized and do not interfere with life or procreation. There are few cutaneous manifestations of heredity that

are so simple, and none so well understood, but the observations of the last few years are tracing some of the cutaneous anomalies to direct inheritance based on a few simple factors.

The most cleancut of these conditions, as far as heredity is concerned, are such obvious deformities as supernumerary digits and peculiar forms of the ears. It is characteristic of this group that these deformities are present at birth, and do not involve, as far as can be seen, any malformation or dysfunction of any other organ.

There is already an enormous amount of literature on this subject, so great that I shall not even attempt to summarize it. Two of the best articles, with long lists of references, are by Siemens [1] and Leven.[2] It is enough here, to mention skin color, hair color, eye color, various deformities of the nails, epidermolysis bullosa, and hereditary hemorrhagic telangiectasia, all of which are certainly hereditary and apparently independent of disease of other organs. Certain peculiarities of the hair, such as curliness, probably belong in this group also.

In the second group of manifestations, it is difficult to determine whether the visible inherited peculiarity, such as excessive or deficient growth of hair, is due to a peculiarity in the skin itself or to some alteration of function of the endocrine, or of some other, system. Most prominent in this group are xeroderma and allied conditions. There is ample evidence that ichthyosis is inherited; so are congenital ichthyosiform erythroderma and keratosis palmaris et plantaris, but it may well be that these are only the external manifestations of an underlying dysfunction. There is considerable evidence that ichthyosis of various grades, keratosis pilaris, onychogryphosis, keratosis palmaris and other forms of abnormal keratinization have a common basis, and that the form which the deformity shall take depends on another factor which also may be inherited. Animal breeders recognize a factor for the distribution of color, which is clearly shown in the belt of Dutch belted cattle. It may be that in these diseases there is a factor which governs the distribution of normal and abnormal keratinization. It is tempting to look for the cause of epidermal defects in dysfunction of the endocrine system, the influence of which on the development and quality of the skin is well recognized. "Certain endocrine disorders are unquestionably hereditary, or perhaps one may better say, they show familial tendencies" (Cushing [3]). Endocrine dysfunction, however, may take different forms in different members of the family. In cases of disorder of the thyroid gland, for instance, some members are of the hyperthyroid type, while others may be cretinoid. However, although the cretin has an abnormal skin and owes his abnormal skin to an inherited

1. Siemens: Virchows Arch. f. path. Anat. **238**:200, 1922.
2. Leven: Zentralbl. f. Haut.- u. Geschlechtskr. **25**:1, 1927.
3. Cushing: Personal communication to the author.

condition, the factor which is inherited cannot be considered as one which concerns the skin per se. The whole subject is so nebulous that it is impossible as yet to discern the laws that govern these vital processes, but it seems probable that in many families there is an inherited tendency to endocrine dysfunction, and that the cutaneous manifestation of this inheritance will vary with the gland involved and with its excessive, deficient or perverted action. Bloch [4] recently reported two cases of cutaneous diseases dependent on insufficiency of the gonads, aggravated in one of them at least by pituitary dysfunction. Other authors also have reported cases showing the dependence of diseases of the skin on the endocrine system, and it is only by recording these cases in detail, with careful notation of the presence or absence of suggestive symptoms in all other members of the family, that light can be thrown on this obscure problem.

There has probably been as much investigation and discussion of the etiology of psoriasis as of any disease of the skin, and the end is not yet reached. The familial occurrence of the disease is too great to be explained by chance, and to account for it one must assume, (1) infection from a common source or from one case to another in the family, (2) exposure to the same unknown environmental condition or (3) a familial, and therefore hereditary, susceptibility. Of these assumptions, the last is the most probable. The majority of the efforts to trace the hereditary nature of psoriasis have treated it as the expression of a single genetic factor, and this has led to confusion and uncertainty, as the pedigrees gathered are not explicable on any such simple assumption. The most reasonable theory that I have found is that propounded by Bernhardt.[5] He said that it is a congenital hereditary and familial mode of reaction of the skin, which may be made apparent by different exogenous and endogenous agents after the skin has been properly sensitized, probably in many cases, perhaps in all, by endocrine dysfunction. It is important to note that there are three separate and distinct elements in this account of the etiology of psoriasis. The first and most important is the hereditary mode of reaction. It is this which determines the particular response to irritation, the particular skin lesion, which is called psoriasis; in its absence, no amount or kind of irritation or sensitization is able to cause that particular eruption. But this mode of reaction is not enough; the subject may never be subjected to an efficient irritation at the proper time, and so may escape all clinical manifestations of the disease, although capable of handing on to his progeny the same mode of reaction. This is one possible explanation of the many cases in which the disease skips a generation, or appears in collateral lines rather than in the direct line. Bernhardt

4. Bloch, Bruno; and Stauffer, H.: Skin Diseases of Endocrine Origin (Dyshormonal Dermatoses), Arch. Dermat. & Syph. **79**:22 (Jan.) 1929.

5. Bernhardt, R.: Ann. de dermat. et syph. (series 7) **7**:27, 1926.

cited two families in which the disease appeared in both parents and in all the children without exception. In these cases, one may assume that the factor is dominant, and that at least one of the parents was homozygous; or that the factor is recessive, in which case the parents and all the children must be homozygous. As is the case in other hereditary cutaneous peculiarities, there seems to be, in many instances, not only a factor for the production of the condition, but also one for its distribution. For instance, Bernhardt cited instances in which the disease, in one family, is always confined to the same limited region—on the head and hands of a father and two children, on the head and upper part of the right buttock of two sisters. He finds psoriasis associated with other hereditary defects, such as keratosis pilaris, keratosis palmaris et plantaris, congenital malformations of the nails, and defective dentition. If these hereditary defects are the result of endocrine dysfunction, as I believe they are in many cases, they find their place in connection with Bernhardt's assumption of sensitization of the skin by endocrine dysfunction as one of the three elements in the etiology of psoriasis. As excitants of the eruption on a susceptible skin, Bernhardt mentioned a large number of irritants, both internal and external. Among the former are various infections such as follicular angina, vaccination, tuberculosis, dysentery, fish poisoning, iodine poisoning, the injection of antistreptococcus serum or of milk, while among the external irritants he mentioned various forms of traumatism both mechanical and chemical—scratching or friction (as on the hands of workmen)—and stated that by the application of turpentine, iodine, phenol and trichloracetic acid he succeeded in determining an outbreak of psoriasis. He cited an acute attack after treatment for scabies and another after the initiation of a severe course of antipsoriatic treatment in a patient in whom the disease had been quiescent for years. As these irritants do not always produce an outbreak in a psoriatic person, he assumed sensitization of the skin by an endocrine secretion, and stated that tuberculosis and other infections may act by interference with endocrine function as well as by direct action on the skin. As an example of the influence of endocrine secretion, he cited the exacerbation of psoriasis during pregnancy and relief from it during lactation. In his personal observations, he found sensitization due to the thyroid gland in 42 per cent of the cases, to the genital glands in 22 per cent and to the thymus in 21 per cent. He marshalled less evidence for endocrine sensitization than for any other part of his theory; nevertheless, the assumption fits in well with the observed cases of endocrine dysfunction in psoriasis and with the good results which occasionally follow endocrine therapy.

In studying the heredity of cancer, one is immediately struck by the fact, noted by Warthin, that all who have investigated the subject carefully are convinced that there is a hereditary element in the etiology

of the disease, while the opponents of this theory are found among those who are particularly interested in therapy. Little [6] calculated the average expectancy of cancer from the mortality tables of the United States Registration Area, from 1903 to 1912, and compared it with the actual incidence of cancer in children one of whose parents had cancer. In the families studied, when the father had cancer and the mother was free from it, there were 1,717 children, 24 of whom developed cancer, while the normal expectancy was 1.9. In the families in which the mother had cancer and the father did not, there were 1,030 children, of whom 39 developed cancer, whereas the normal expectancy was 2.78. In preparing the statistics, the age of the patients was considered. The discussion of the heredity of cancer is no longer concerned with the fact but rather with the explanation of the mode of inheritance. On two points, all the investigators seem to be in agreement; (1) that there is an inherited tendency to this mode of reaction, and (2) that some form of stimulation is necessary for the actual development of the disease. In very susceptible persons, this stimulus may be so slight that the disease appears to be spontaneous, while in the very resistant subject, prolonged and severe irritation may be required. The mode in which this susceptibility is inherited is still under discussion. Maude Slye expressed the belief that the cancer-resistant mechanism, the tendency to react to any injury by normal growth and healing, is dominant, and that the essential feature of cancer is the absence of this tendency to normal proliferation. In the absence of this "mechanism for controlling growth and differentiation in regenerative processes," cancer may develop. The susceptibility to cancer, being the absence of a mechanism for controlling growth, must therefore, on the presence and absence theory, act as a recessive. Dr. Slye claimed that all her experiments support this assumption. As she acknowledged that "individuals may vary greatly in their cancer resistant mechanism," it would seem that there must be several factors involved in normal resistance to cancer. Putting aside this question of interpretation, the fact remains that by selective mating she was able to produce families of mice in which nearly 100 per cent developed cancer, if they lived to cancer age, and other strains in which cancer never occurred. Other workers have developed susceptible and resistant strains, but do not claim to have carried either to an homozygous condition. Dr. Slye [6a] said that in the susceptible strains, a blow or a wound is regularly followed by cancer, while in an individual of a resistant strain the area receiving the same injury heals normally. This statement, taken by itself, is too

6. Little: Carnegie Institution of Washington Year Book 20, Washington, D. C., 1921, p. 139.

6a. Slye, Maud: J. Cancer Research **11**:135, 1927.

broad, and needs qualification. Slye said that if an injury is inflicted on a susceptible member of a family susceptible to cancer of the breast only, no tumor results if the tissues of the breast are not injured. If the individual is a member of a family susceptible to cancer of the skin only, the blow frequently occasioned cancer of the skin in the injured region. Dr. Slye said further that even susceptibility to cancer of the skin may be localized: If a mouse susceptible only to cancer of the skin of the face was struck anywhere except on the face, normal healing took place. Many strains of mice that never showed mammary gland carcinoma produced 100 per cent of tumors of the lung. This inheritance of cancer as a disease of a single organ or tissue rather than as a general condition, has been noted by other workers. Lynch [7] experimented with two strains of mice; one showed a very large percentage of cases of cancer of the breast, and a small percentage of cancer of the lung, while the other showed comparatively little cancer of the breast, but a large percentage of cancer of the lung. She did not give the incidence of spontaneous cancer of the skin in either strain, but said that counting all cases of cancer together, no matter of what organ, the first strain was nearly three times as susceptible as the second. Nevertheless, the two strains were equally susceptible to the production of cancer by painting the skin with tar. The experiment proves only that susceptibility to cutaneous tar cancer is independant of susceptibility to cancer of the breast or lung. Later she [8] varied the experiment. It had been reported by Murphy and Sturm [9] that painting the skin of various parts of the body, one after another, for a considerable period of time would lead to the development of the lung cancer in suitable cases, while the irritation of the skin in any one spot might be so slight as to avoid the development of cutaneous cancer. The mode of action of tar in this case is not explained, but the fact is as given. In the first strain mentioned, about 7 per cent of the individuals developed tumor of the lung spontaneously, while 22 per cent developed tumor of the lung following painting with tar. In the second strain, over 37 per cent developed tumor of the lung spontaneously while 85 per cent developed tumor of the lung after cutaneous painting. These two strains were crossed, and 75 per cent of the first filial generation developed tumor of the lung after painting with tar. When this filial generation was back-crossed to the susceptible strain, 81 per cent of the offspring developed tumor of the lung after painting with tar, but when back-crossed to the relatively resistant group, only 39 per cent developed tumor of the lung after painting with tar. The result indicates that susceptibility to

7. Lynch: J. Exper. Med. **42**:829, 1925.
8. Lynch: J. Exper. Med. **46**:917, 1927.
9. Murphy and Sturm: J. Exper. Med. **42**:693, 1925.

tar-induced tumors in the lung is hereditary. Warthin[10] said that some human families show cancer in only one organ; e. g., the stomach, the thyroid, the lip. He gave an interesting example which illustrates also the importance of the extrinsic factor, the irritant, in the production of the disease. Four brothers showed multiple incidence of cancer in their forebears. Unfortunately, it was not recorded what form cancer took in the ancestry. Of these four brothers, three were smokers, and died in middle life of typical smoker's cancer of the lip. The fourth brother never smoked, and had absolutely no history of injury or chronic irritation to his lip; at 65 years of age, however, he developed spontaneous cancer of the lip—twenty-five years later than did the smoking brothers. Warthin expressed his belief that a general constitutional and a local organ or tissue predisposition are the principal genetic factors concerned, and that clinical and pathologic evidence points to dominance rather than to recessiveness in the inheritance of this susceptibility. To sum up, there is a general agreement that (1) local organ or tissue susceptibility to cancer is hereditary; (2) there may be a general or systematic susceptibility, but this is uncertain; (3) this susceptibility varies in its degree, and (4) many susceptible persons may escape the disease from the lack of any sufficient excitant.

It would seem to me that the most reasonable explanation is that resistance to cancer, which is the same thing as normal control of growth and regeneration, is the result, not of a single factor, but of many dominant factors, and that as these factors are lost, the individual becomes more and more susceptible to the disease until a state is reached—as exemplified in some of Dr. Slye's mice and in some of the families studied by Dr. Warthin—in which the development of the disease is inevitable if the patient lives long enough.

The importance of heredity in the allergic group of diseases is recognized by all who have studied the question. Cooke[11] stated that data collected from several hundred normal persons showed an antecedent history of allergy in 7 per cent, whereas 796 allergic cases gave a positive antecedent allergic history in 58 per cent. In the group in which inheritance could be traced through both father and mother, symptoms of allergy began before the tenth year in 75 per cent; when the inheritance was single, in only 30 per cent, while in the group in which no inheritance was evident, in only 20 per cent. Of all children with bilateral allergic inheritance, about 70 per cent will become allergic, while of those with unilateral inheritance about 50 per cent will become allergic. The percentage of cases is greater and the age at onset younger in families in which there is a history of allergic disease on both the

10. Warthin: J. Cancer Research **12**:249, 1928.

11. Cooke: M. J. & Rec. **122**:537 (Nov. 4) 1925.

paternal and maternal sides, than in those which give such a history on one side only. Balyeat[12] stated that "in a study of 1117 normal university students, it was found that a positive family history of hay fever and asthma occurred in relatives of the first degree in only 8.3 per cent, which is in marked contrast to such a history found in 60.1 per cent of patients suffering with hay-fever and asthma." He expressed the belief that the tendency is inherited as a simple dominant. It is to be noted that the importance of heredity in this group is based on diseases the allergic character of which is unquestioned: hay-fever and asthma. The same authors observed in these allergic families an abnormally large percentage of cases of urticaria, Quincke's edema and eczema, diseases which in many instances are now proved to be allergic in origin. The data are still insufficient to prove the mode of inheritance, but it seems to be established that what is inherited is a capacity to become sensitive to certain foreign substances, not necessarily protein. This transmitted capacity is not specific: The parent may be sensitive to ragweed, while the child may become sensitive to rabbit fur; the parent may react by an attack of asthma, the child by urticaria. It is not necessary, therefore, to assume the limitless number of factors that would be required for the inheritance of specific sensitivity. The particular sensitivity that develops depends on the surroundings of the individual, but why one tissue rather than another should be sensitized is still uncertain. These researches have opened up an entirely new field in the study of the heredity of diseases of the skin and call for carefully taken history in all cases of eczema, urticaria, and erythema, in an effort to discover in the ancestry and the collaterals, instances not only of these dermatoses but also of hay-fever, asthma and allied conditions.

The heredity of infectious disease, or rather susceptibility to infection, concerns the dermatologist as much as it does any other physician. Most clinicians get the impression that some families are resistant to infection, always in sturdy good health, while others are always ailing, picking up any disease that may come along; but such general impressions need careful examination and verification before they can be accepted. Up to the present time, most of the experimental work in this line has been done by botanists who have developed strains of wheat and corn which are more than ordinarily resistant to various blights, and have been able to fix this resistance as an inheritable quality. The same phenomenon—the inheritance of variations in susceptibility—has been noted by zoologists. Slye said[13] that from her own laboratory experience it seems reasonably certain that the tendencies

12. Balyeat: Am. J. M. Sc. **176**:332 (Sept.) 1928.

13. Slye (footnote 6a).

to susceptibility and immunity have an hereditary basis, but that in no case which she had been able to test had these tendencies behaved like presence and absence unit characters. Wright and Lewis [14] studied the resistance of pure bred guinea-pigs, developed by continuous brother and sister matings, against infection with the tubercle bacillus; they found demonstrable differences, evidently inherited. They considered that several factors were involved. Webster [15] carried out a careful series of experiments with strains of mice which had been maintained several years in the laboratory, and whose susceptibility to mouse typhoid could be measured by a fairly constant percentage. All were kept under identical conditions of heat, ventilation and feeding, and a selected group were infected with mouse typhoid by administering a measured dose of culture by mouth. Certain of the survivors who were proved to have no typhoid bacilli in their excreta and no specific agglutinins in the blood were then mated, and their offspring were again infected with typhoid. This first filial generation was distinctly more resistant to typhoid than the ancestral stock, as shown by a lower death rate. Survivors of this first filial generation were then mated, and their offspring tested in the same way. This second filial generation showed a distinctly lower death rate than the first. The experiment proved that resistance to mouse typhoid is a hereditary quality. Webster tested these typhoid-resistant mice against poisoning by bichloride of mercury, and found that they were more resistant to this metallic poison than were the general stock. He also stated that "mice which survive a preliminary dose per os of paratyphoid enteritidis bacilli are more resistant to a second dose per os of a similar (not necessarily identical) epidemic mouse typhoid strain than are mice which have received no preliminary culture, and that the amount of this resistance is related to the pathogenicity of the preliminary strain more than to its antigenic similarity to the second strain." This resistance is therefore not entirely a specific quality; mice that are resistant to one type of typhoid infection are resistant to other types also, and what is more remarkable, they are more resistant to a metallic poison (mercury) than are average mice. This is a most important observation in view of the fact that allergic irritability, previously discussed, is not specific, but general. Later he [16] extracted strains distinctly more susceptible than the average, and proved that this high susceptibility is hereditary. Both the controls, the resistant and the susceptible strains, showed seasonal variation in susceptibility. He concluded: "Whatever the potential inherited constitution of individuals, families or races may be,

14. Wright and Lewis: Am. Naturalist **55**:20, 1921.
15. Webster: J. Exper. Med. **39**:129 and 879, 1924.
16. Webster: J. Exper. Med. **42**:1, 1925.

it is affected profoundly by seasonal influences, food and general hygenic conditions. For this reason it is erroneous to speak of the presence or absence of resistance as though it were a unit factor. Rather it is to be considered a manifestation of an extremely complex mechanism, modified by heredity and environment."

These two qualities, inherited allergic irritability and inherited resistance to infection, both of which, in part at least, appear to be general rather than specific, may well be related to each other. Decamps [17] tested 120 subjects by repeated injections of small amounts of horse serum, and found that 1 per cent gave no response—they had no defense mechanism—95 per cent always gave a reaction, while 4 per cent attained immunity. The same subjects, tested with milk and with tuberculin gave the same results, whence he drew the important conclusion that a subject endowed with a susceptibility to one protein substance shows himself, in the same manner, capable of every other sensitization. Decamps then considered allergic response in syphilis. Toward the third year, in the majority of cases, the disease limits itself to a few massive lesions, localized in a single tissue, as in gummas, but in other cases it remains an ultrachronic infection, widely scattered in numerous tissues, as manifested in late secondary lesions, paresis, tabes and vascular syphilis. The first are the allergic cases, with great capacity for sensitization; among these is found the faculty of fixation and even of spontaneous cure of the infection, while the second class (e. g., the tabetic patients) are anallergic and are those which have given the most convincing examples of absent or feeble capacity for sensitization, either to horse serum or to cow's milk. This general feebleness of reaction is the cause of the persistent and progressive character of the disease. If the course and the manifestations of syphilis depend, partly at least, on the allergic or nonallergic character of the individual, and if allergic irritability is a hereditary quality, it follows that in syphilis the mode of reaction to the infection depends, partly at least, on the hereditary constitution of the individual. Approaching this problem of the relationship between resistance to infection and allergic irritability from a different direction, Balyeat [12] arrived at the same conclusion. Basing his studies on 1,217 patients with hay-fever, asthma and allied conditions, he said that nearly 75 per cent of them were above the average in general health, especially in resistance to infection.

Although one is compelled to accept resistance and susceptibility as hereditary qualities, sufficient data are still lacking to establish the mode of inheritance; in particular, extended and well authenticated genealogic tables, whether for man or animals. Another difficulty in

17. Decamps: Bull. Soc. étude d. formes humaines, 1926, p. 145.

interpretation arises from the fact that there are so many grades between the two extremes that one cannot account for them by the presence or absence of a single factor; the difficulties of analysis increase rapidly with every increase in the number of factors to be considered. These are problems for the experimenter and the professional geneticist.

What is the interest of the practicing dermatologist in all these matters? In the first place, he will learn to recognize certain so-called diseases as innate peculiarities which cannot be cured. Some may be removed, like superfluous digits, while others, like hereditary hemorrhagic telangiectasis, can only be alleviated. In the second place, as knowledge of the influences of endocrine function on the skin and of the inheritance of endocrine disturbance becomes more accurate, one may learn to ascribe many of the inherited cutaneous anomalies to this cause and perhaps to give treatment for them. In the third place, a family history of typical allergic diseases like asthma and hay-fever is a warning to be on the lookout for the eruptions which belong in the same group. Lastly, a knowledge of the heredity of diseases of the skin may be of great value in dealing with patients suffering from them, who always want to know if their children will be victims of the same curse. An exact answer can seldom be given, but the more nearly complete the physician's knowledge, the greater will be his confidence in reassuring his questioner in some cases, or in explaining that though a disease belongs in the hereditary group, the chances of an individual child suffering from it may be very small. But when all is said, the real and abiding interest in such studies is found in the light which they throw on otherwise insoluble problems.

ABSTRACT OF DISCUSSION

PROF. JADASSOHN, Breslau: I find it difficult to enter a theoretical discussion on this complicated subject, which was treated in these interesting lectures, and therefore I want to make a few remarks from a clinical standpoint only.

I have always found it important to study heredity, not only in the rare anomalies of the skin but also in the more common diseases, as mentioned by Dr. Williams, e. g., psoriasis; but it is not sufficient to give the number of cases in which heredity seems to be proved, it is necessary also to give the special qualities of the single cases. So I found occasionally that in one family only a few members were psoriatic, and that the same, and only the same, were diabetic, while in a general way I could not find special relations between psoriatic and diabetic cases. In one family I could find only an uncle and a nephew with psoriasis. They resembled each other in a striking manner; they had the same form of psoriasis; they were both fat, and they were both cured by internal doses of arsenic in such a short time that I myself was astonished. If we pay attention we shall perhaps be able to find that the so-called constitutional factor in psoriasis may be combined with other constitutional or hereditary factors.

Also in other diseases of the skin with unknown causes we often ask if the condition is hereditary or infectious. Of course both factors may play an important rôle together. Many years ago I found that among cases of lichen planus

occurring in the same family those of consanguineous persons are much more frequent than those occurring in husband and wife, while the chances of contagion are of course much greater in the latter. So far as I see, that was confirmed also later on. This fact speaks in the sense that in case lichen planus would be an infectious disease or a hereditary or constitutional predisposition is much more important in the etiology than the infectious factor. The same seems to be true of alopecia areata.

I want to quote also the gonorrheal arthritis. We know of cases of occurrence of this disease; for instance, when brothers are infected from different persons; on the other hand, the same strain of gonococci may produce arthritis in nonconsanguineous persons. That is, even in an infectious disease both must be studied, i. e., the heredity and the special quality of the races of microbes. Also in syphilis this point of view is important. For instance, parenchymatous syphilis of the nervous system, we may say, sometimes has a special predisposition and sometimes a special strain, or both.

Finally, I should like to mention the heredity of vitiligo. I found only a few cases, but one of them was interesting, because mother and daughter both had the first lesion localized in the same region and beginning at the same age.

DR. SCHAMBERG, Philadelphia: I have listened with great pleasure and profit to the splendid presentation of Professor Leake and the admirable paper of Dr. Williams. A subject of this sort is attended with extreme difficulties by reason of absence of knowledge of hereditary factors and by reason of the still imperfect knowledge of many dermatitides.

I was struck, as was Professor Jadassohn, by the suggestion that psoriasis is a disease of hereditary character. I cannot adhere to this point of view. You may recall that some years ago I reported careful studies of 600 private patients in whom the disease was carefully investigated as to its existence in other members of the family. As I recall, there were seventeen instances of psoriasis in collateral branches of the family, leaving eighty-three in which there was none. Furthermore, in only 5 per cent was there a history of psoriasis obtainable in either father or mother, so if in 95 per cent we obtain no evidence of psoriasis in either parent we have rather slender evidence on which to base a thesis of heredity. I reported two cases of a husband having psoriasis, the wife having previously suffered from it.

The cause of psoriasis is not known; whether it is metabolic, infectious or of endocrine origin must still be cleared up, but I cannot endorse the hereditary view of psoriasis. If other figures corroborate those which I published it seems to me that we have entirely inadequate evidence on which to predicate such a view.

I believe that the papers which have been presented are of great value, and that a more careful reading of them will increase our appreciation of the subject.

DR. PUSEY, Chicago: I think that Dr. Williams' paper is especially significant because he has reviewed what we know of heredity in skin diseases in the light of Mendel's law. I believe that we have had no former paper in the Association which has considered heredity in dermatology from this standpoint. I do not see how we can go further in discussing Dr. Williams' paper than to express our recognition of this fact, for any discussion of heredity in the light of Mendel's law requires so close reasoning that, so far as I am concerned, the only way in which I can follow it is to take pencil and paper and chart my course. It is not a subject that can be discussed in any casual way. I wish also to express my appreciation of Dr. Leake's clear statement of what we now know of the laws of heredity.

DR. WEIDMAN, Philadelphia: When we come to an ephemeral subject like this I think that we should start with definitions. Approaching it as dermatologists, we are likely to think of it, loosely, in connection with conditions occurring in children which have occurred in parents. But as I recall it, true heredity must involve the germ plasm, and the failure to appreciate this lies at the basis of a great deal of the discussion pro and con whether some diseases are hereditary, congenital or familial. We are all aware of the bandying of these different terms, particularly in connection with syphilis. As I understand it, up to the present there has been no proved instance in which the spirochete has been demonstrated in or on the microgamete; therefore, if we continue to employ terms which the biologist has handed down to us we must continue to use the terms congenital or hereditary in their original sense, as the case may be. At the same time we must remember that there are certain characters handed down to the offspring that are not of the chromosome; Adami exposes this most charmingly in his text on general pathology (General Pathology, ed. 2, Philadelphia, Lea & Febiger, 1910, vol. 1, pp. 210 and 205) when discussing the inheritance of diatheses versus the inheritance of infections. The stigmas of alcoholic, tuberculous and syphilitic parents are illustrative. We should not think of heredity only in connection with the chromosome—there are factors also in the cytoplasm.

I should like to ask Dr. Leake for the explanation of the transmission of characteristics, mutation for instance, in those cases in which the particular form of life is anuclear, as in lower fungi. Here the nuclear substance is widely dispersed, and it is scarcely conceivable that transmigration of genes could take place in any sort of an orderly way. In short, there is more than one consideration showing that the matter of heredity is concerned with other factors in addition to the migration of chromosomes.

Finally, coming down to the clinical side, what is the approach to the more exact understanding of what is going on in a given dermatosis, suspected as hereditary? That is, as we approach a given dermatosis, say ichthyosis, in what terms should we think of that condition? We should first determine the particular elements in the skin which are concerned and after that the pathologic process that is taking place; after that, the anamnesis. In a case of familial telangiectasia it would be blood vessels first and after that, not metabolic observations, but the more tangible factors in the case, such as weakness of the blood vessel walls, blood pressure and so on. If we proceed in this way we can hope to improve our dermatologic nomenclature, supplementing "purpura" with more meaningful terms like "hereditary vascular weakness," hereditary thrombocytopenia," "hereditary hyperpiesis," and so on.

I think that we are all agreed that we have been informed both from the biologic and from the clinical side. The biologist of the past has had the easier road. With ample, easily controlled materials he has been able to begin with genes and work upward, and now with the information the medical man has given him he is in the position to work backward and fit the clinical circumstances into his schema genetica.

DR. LANE, Boston: This spring I had an opportunity to listen to Professor Parker, professor of zoology at Harvard University, on this subject and in his discussion of heredity he spoke interestingly of identical twins, meaning those twins that have resulted from fertilization of a single ovum and who, therefore, look alike and act alike. He commented particularly on a study that was being made of dementia praecox in these twins. He quoted one case; in the discussion, a neurologist mentioned six cases of dementia praecox, all occurring in one twin, the other having been found to have either beginning dementia praecox or to have

been committed for it. Thus, in this particular disease it can be said that there is a definite disturbance of the germ plasm. It occurred to me that if any one of us has an opportunity to study diseases of a suggestive congenital origin, or of an uncertain origin in twins, there would be the possibility of making some contribution to the side of heredity.

DR. POLLITZER, New York: One thing strikes me as a possible conclusion from the admirable papers and the excellent discussion, and that is the importance of making careful records, especially when dealing with intelligent patients who know more about their grandparents and their parents than the average person knows. In that way we can perhaps gather some material which will be comparable in value to the material gathered in the laboratories, where we deal with mice and sweet peas. A great disadvantage under which we labor is the lack of material. Families are small and generations are long, but hereditary factors play a rôle in skin diseases though opportunities for observation may be rare. In the experience of every physician there are occasional instances that show that familial disease conditions exist, the careful recordation of which and the accumulation of which in suitable archives would form a basis from which valuable deductions might be made.

An instance in my experience was that of a child seen several years ago. The child was brought to me for total alopecia of the scalp, and I found that the child was a member of the fourth generation in every one of which this condition had occurred in at least one member. The great-grandfather suffered from the same disease. He had been born with apparently normal hair which all fell out at 5 or 6 years. There was a moderate return of the coarse hair which in turn fell out after a year or two. A similar condition had existed in one or more members of each succeeding generation. My patient was the only child of her parents. A careful examination by endocrinologists and neurologists resulted in a rather vague report that there was a general endocrine dysfunction.

This is not of much value as a single instance, but I mention it as an illustration of what I have in mind, that we do occasionally get cases in which careful study of the history may be of importance, and if similar records were gathered in large quantities we should have something comparable to the laboratory experiments.

DR. COLE, Cleveland: I think that it has been appropriate that the society should bring up the subject of heredity for discussion. There is no question but that we as dermatologists can learn a great deal from a study of heredity. We have been fortunate in hearing Professor Leake, who has given us a great deal of information.

How many diseases do we have in dermatology that are hereditary? I think that the Americans have not laid as much stress on this as the French and German workers; e. g., Bettmann in Schwalbe's monograph, "Die Morphologie des Missbildungen," which is exceptional in showing the numerous dermatologic conditions that are hereditary. We are constantly encountering one condition or another that is certainly hereditary, and only by making careful notes can we get a better idea regarding them. It has been of great benefit to have these talks by Professor Leake and Dr. Williams.

DR. GRINDON, St. Louis: I wish to second Dr. Pollitzer's remark that such observations should be put on record even if they make no more than twenty lines. I feel that much is lost by not communicating such observations in the ARCHIVES, so that they may be preserved. I hope that you will all remember this and put such data on record.

PROF. LEAKE, University of California: I do not think that anything is known with regard to mutation in fungi. I do not believe that fungi have been studied from this particular standpoint. It is possible that inherited factors which may make up an individual may be transmitted by other factors than the chromatin tissue.

Let me echo Dr. Pollitzer's remarks with the suggestion that you appoint a committee, if only one person, to receive from the various members of the organization, if you are really interested in the heredity of skin diseases, the actual case histories and family pedigrees. Let the committee, when a sufficient number of histories has been received, make a report and turn this material over to a geneticist. You may get something of great value.

DR. WILLIAMS, New York: Dr. Schamberg's remarks would indicate that he considers psoriasis as due to a single cause, the presence of which inevitably produces the disease, which is a conception I tried to prevent. There may be several factors, and the fact that only collaterals are affected and generations are skipped does not mean that the disease is not hereditary. The hereditary tendency may exist and may remain latent. Also, cases in the family may easily be overlooked or be forgotten. We have all seen cases in which there were only small patches on the elbows or on the glans penis: What is the grandchild to know of these few patches?

Regarding a committee to receive reports of examples of heredity, there is already such an organization in existence. The Genetics Record office at Cold Spring, N. Y., is eager to get such histories, and will welcome anything you may send in. What they want is carefully worked out charts, which must include not only the affected members of a family but the unaffected members as well.

Another point I wish to emphasize is the fact that skin diseases as yet are not well classified. Most of our classifications are on clinical forms, and it may be that diseases which appear different clinically have the same hereditary basis. Many cases of eczema and of urticaria appear to belong in the hereditary group, occurring in families some of the members of which have asthma or hay-fever. As they may all be expressions of the same hereditary constitution, it is important that histories should not confine themselves to dermatoses.

STUDIES OF INORGANIC SALTS OF THE BLOOD IN PSORIASIS *

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Psoriasis is a disease of such obscure etiology that any investigations concerning it are worthy of publication. There is a factor that influences the activity or the quiescence of the eruptive manifestations in this disease. While numerous investigations along metabolic, bacteriologic and other lines have been intensively carried out, no dogmatic utterance as to the exact nature of psoriasis can at the present day be made.

We examined the blood of twenty patients in various stages of activity for the calcium-potassium ratio and for the content of magnesium and phosphorus. These inorganic constituents of the blood did not materially depart from normal values.

The normal figures for calcium, magnesium, potassium and phosphorus we take to be as follows:

Calcium	9 to 11 mg. per 100 cc.
Magnesium	1 to 2 mg. per 100 cc.
Potassium	18 to 20 mg. per 100 cc.
Phosphorus	2 to 4 mg. per 100 cc.

The technic employed was as follows: Tisdall's modification [1] of Kramer and Tisdall's [2] method was used for the calcium determinations. Magnesium was determined on the supernatant fluid from the calcium oxalate precipitate according to Denis.[3] Potassium was determined by Kramer and Tisdall's [4] method, and the phosphorus results were obtained by the method of Benedict and Theis.[5]

* Submitted for publication, Nov. 15, 1929.

1. Tisdall, F. F.: J. Biol. Chem. **56**:439, 1923.
2. Kramer, B., and Tisdall, F. F.: J. Biol. Chem. **47**:475, 1921.
3. Denis, W.: J. Biol. Chem. **52**:411, 1922.
4. Kramer, B., and Tisdall, F. F.: J. Biol. Chem. **46**:339, 1921.
5. Benedict, S. R., and Theis, R. C.: J. Biol. Chem. **61**:63, 1924.

Study of Inorganic Constituents of Blood

No.	Name	Date	Age	Sex	Diagnosis	Ca	Mg	K	P	Remarks
1	N.	6/ 5/28	..	M	Psoriasis	9.7	1.5	....	2.5	Resistant and active (slight hemolysis)
2	S.	6/ 6/28	60	M	Psoriasis	10.1	1.2	17.8	1.7	Active; moderate
3	F.	6/15/28	..	M	Psoriasis	10.5	2.7	15.6	4.1	Very active; moderate
4	C.	6/18/28	62	M	Psoriasis	10.0	2.0	16.2	3.6	Beginning active, not extensive
5	N.	6/18/28	38	F	Psoriasis	10.0	1.3	16.0	3.5	Active, fairly extensive
6	A.	6/18/28	48	M	Psoriasis	11.2	1.9	15.6	3.1	Moderate, not active
7	K.	6/20/28	37	M	Psoriasis	9.6	1.7	18.3	2.8	
8	S.	6/21/28	30	M	Psoriasis	10.8	2.2	19.8	2.8	
9	W.	6/25/28	..	F	Psoriasis	9.2	1.6	17.2	3.6	Relatively scanty, new lesion
10	B.	6/25/28	..	F	Psoriasis	10.8	2.0	18.6	4.2	Practically no eruption present
11	R.	6/25/28	..	F	Psoriasis	11.4	1.9	16.6	2.8	
12	W.	6/26/28	49	M	Psoriasis	10.0	2.0	17.6	1.9	Moderate eczema
13	J.	6/27/28	..	M	Psoriasis	9.5	2.1	17.3	3.2	
14	B.	6/27/28	..	M	Psoriasis	10.9	1.7	17.8	3.4	
15	B.	7/10/28	33	M	Psoriasis	10.2	1.8	18.8	3.7	
16	P.	10/ 8/28	55	F	Psoriasis	10.5	1.1	21.3	3.0	
17	C.	10/ 8/28	..	F	Psoriasis	10.0	1.2	....	2.8	
18	A.	10/ 8/28	29	M	Psoriasis	9.2	1.7	17.1	...	
19	S.	10/ 8/28	25	M	Psoriasis	10.8	1.5	....	...	
20	L.	10/31/28	..	F	Psoriasis (acute)		...	....	2.6	

ABSORPTION RATE OF BISMUTH COMPOUNDS*

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Since its introduction in 1921, by Sazerac and Levaditi, bismuth has rapidly proved its value as an antisyphilitic agent. Many articles have been written attesting to its great worth in patients, and also in animals experimentally infected with syphilis. As in the case of many new remedies some of the early reports have been ultra-enthusiastic. There are at present a number of different salts or compounds of bismuth on the market, so many, in fact, that it is difficult for a physician to evaluate properly the claims made for these various brands and to choose one to use in his practice.

A great deal of work remains to be done in regard to the pharmacology, toxicology and therapeutics of the bismuth preparations. We have attempted to aid in only one phase of this complicated problem, namely, in studying the absorption of the various brands of bismuth by means of roentgen examination of patients and experimental animals. This is not a new field, others having explored it previously, but we hope to throw more light on compounds already studied and to present studies of other compounds not included in previous investigations. The observations of previous investigators are briefly reviewed in the subsequent material.

OBSERVATIONS ON VARIOUS BRANDS OF BISMUTH BY PREVIOUS INVESTIGATORS

Potassium Bismuth Tartrate.—Erdman [1] found that in one patient potassium bismuth tartrate remained unabsorbed after three hundred

* Submitted for publication, Aug. 27, 1929.

* Read before the Section on Dermatology and Syphilology at the Eightieth Annual Session of the American Medical Association, Portland, Ore., July 11, 1929.

* From the Departments of Dermatology and Syphilology of the Baby Hospital, Oakland, Calif., The Alameda City Health Center, Alameda, Calif., and Fairmont Hospital, Oakland, Calif.

1. Erdman, Bernhard: Is Bismuth Absorbed? J. A. M. A. **92**:1252 (April 13) 1929.

and forty-seven days. He did not state whether or not injections of other brands of bismuth or mercury had been previously given, which obviously is a vital consideration. Beinhauer [2] found that it was absorbed after eight weeks. Cole [3] studied this drug in nine patients (thirty injections were studied). Twenty-two of the thirty injections were absorbed in fourteen days; seven injections failed to be absorbed in fourteen, twenty, twenty-two, twenty-four, twenty-nine, twenty-nine and thirty-nine days, respectively.

Bismuth Subsalicylate.—Erdman [1] found bismuth subsalicylate unabsorbed after two hundred and four days in one patient. As in his report on potassium bismuth tartrate, he did not rule out the possibility of previous injections of some other bismuth or mercury salt giving rise to the shadows.

Bismuth Salicylate.—Beinhauer [2] found that bismuth salicylate was absorbed after nine weeks.

Cole [3] found that in ten of forty-four patients this drug had absorbed in a mean of forty-four days. In the other thirty-four patients, it was not absorbed in periods varying from fourteen to one hundred and twenty-four days.

Sodium Bismuth Tartrate.—Erdman [1] found that all traces of sodium bismuth tartrate had disappeared twenty-one days after the last of ten injections had been given.

Metallic Bismuth.—Wolfer [4] injected 1 cc. (0.06 Gm.) of metallic bismuth into three rabbits. In one a shadow was seen in the x-ray picture after twenty-six days; in the second rabbit, complete absorption occurred in thirty-seven days; in the third rabbit a shadow was present after twenty-three days.

Beinhauer [2] found that one brand of metallic bismuth (neotrepol) was absorbed in five weeks.

Cole [3] found that metallic bismuth (B. W. & Co.) showed no evidence of absorption in forty-four days in one patient and in one hundred and fifty days in another.

Bismudol (Phenyl Formitate of Bismuth).—Beinhauer [2] reported absorption of phenyl formitate of bismuth after six weeks.

Iodobismuthate of Quinine.—Beinhauer [2] reported that iodobismuthate of quinine was absorbed after four weeks.

Bismuth Oleate.—Cole [3] followed nine patients who had received injections of bismuth oleate for periods varying from twelve to sixty-eight days and found no evidence of absorption.

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2. Beinhauer, L. G.: Pittsburgh M. Bull., March 28, 1925, p. 9.

3. Cole, H. N.; Miskdjian, H., and Farmer, H. L.: Intramuscular Absorption of Some Insoluble Bismuth Compounds as Revealed by the Roentgen Ray, Arch. Dermat. & Syph. **13**:219 (Feb.) 1926.

4. Wolfer, P.: Schweiz. med. Wchnschr. **3**:703, 1922.

Bismuth Oxybenzoic Acid.—Cole [3] found little or no absorption after forty days in one patient and after forty-four in another.

REPORT OF STUDIES ON PATIENTS

In our various clinics, injections of different bismuth preparations were made intramuscularly into patients. Most of these injections were given into the outer upper quadrant of the buttocks, the technic described by Stokes being used. A few received injections into the deltoid muscles. In all instances both in patients and in experimental animals active muscles were chosen as the sites of injection, as Gruhzit [5] had shown that there is a marked difference in the rate of absorption of bismuth from active and passive muscles. The dosages used on patients were those recommended by the manufacturers. A total of 136 injections of seventeen various compounds were studied. An attempt was made to make roentgen studies of the patients at regular intervals until the bismuth deposits had disappeared, but because of irregular attendance at the clinics, the pictures in some could not be taken as soon as we would have desired. This means that some of the deposits which showed complete absorption at a certain time might have shown complete absorption a week or two earlier had we been able to secure a picture. This applies particularly to the rapidly absorbed water-soluble products.

WATER-SOLUBLE PREPARATIONS

Bismosol.—Thirteen patients were given injections of bismosol, a dextrose-aqueous solution of potassium sodium bismuth tartrate. A faint trace remained after two hours in one patient. Three other injections had completely disappeared in two hours. All had entirely disappeared within fourteen days.

Thiobismol.—Seven patients were given injections of thiobismol, an aqueous solution of bismuth thioglycollate. Three of these showed complete absorption after two hours. Roentgenograms were not taken of the other four until after thirteen, thirteen, fourteen and thirty-three days, when no bismuth could be found.

Sodium Bismuth Tartrate.—Eight patients received injections of sodium bismuth tartrate in aqueous-sucrose solution. That it was rapidly absorbed was evidenced by two patients in whom none could be found after one and two hours, respectively. Roentgenograms were taken of six other patients at intervals varying from seven to twenty days, but no unabsorbed bismuth remained.

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5. Gruhzit, O. M.: Bismuth Salicylate in Experimental Rabbit Syphilis, Arch. Dermat. & Syph. **13**:195 (Feb.) 1926.

Bismarsen.—Ten patients were given bismarsen, an aqueous solution of bismuth arsphenamine sulphonate. Faint traces were seen immediately after injection and could be followed in two patients for seven and sixteen days. All of the other eight injections showed complete absorption in periods varying from five to twenty-four days.

SUSPENSIONS

Bismoid.—Nine injections of bismoid, a dextrose-aqueous suspension of bismuth, were studied. Two injections were completely absorbed

TABLE 1.—*Results of Injections of Bismosol* *

Patient	Sex	Age	Number of Injections	Interval	Dose	Date of First Injection	Date of Last Injection	Date and Number of Roentgenogram	Time from Last Injection to Roentgenogram	Absorption
Mrs. K.	F	..	4	W	0.1 Gm.	3/ 6/29	3/27/29	4/ 3/29 A9305	7 days	Complete
L. K.	F	6	1	..	1 cc. deltoid	3/14/29	.....	3/14/29 B4525	2 hours	Complete
M. G.	M	..	10	W	1 cc.	1/16/29	3/20/29	3/27/29 A9259	7 days	Complete
J. K.	M	..	1	..	1 cc. right deltoid	3/14/29	.....	3/14/29 B4527	2 hours	Faint trace
M. K.	F	9	1	..	1 cc.	3/14/29	.....	3/14/29 B4526	2 hours	Complete
E. M.	M	6 mo.	1	..	0.25 cc.	3/21/29	.....	3/21/29 B4329	2 hours	Complete
E. E.	F	22	1	..	1 cc.	3/29/29	.....	3/29/29 B4589	2 hours	Complete
B. L.	F	26	1	..	1 cc.	3/ 9/29	.....	3/16/29 T11468	7 days	Complete
J. L.	F	25	1	..	1 cc.	3/ 9/29	.....	3/12/29 T11459	3 days	Complete
M. G.	M	50	10	W	1 cc.	1/16/29	3/20/29	3/27/29 A9259	7 days	Complete
M. K.	F	..	10	W	1 cc.	3/ 6/29	5/ 8/29	5/22/29 A9552	14 days	Complete
C. H.	M	33	1	..	1 cc.	6/ 5/29	.....	6/12/29 T11685	7 days	Complete
E. M.	M	9 mo.	1	..	0.25 cc.	5/16/29	.....	6/13/29 B4913	28 days	Complete

* Bismosol is a dextrose-aqueous solution—potassium sodium bismutho-tartrate. (It is identical with a product originated by Poulene Frères, Paris—per manufacturer.) One cubic centimeter of bismosol is equivalent to 0.10 Gm. of potassium sodium bismutho-tartrate (manufacturer's statement). (Put up in 1 cc. ampules.) The amount of bismosol per cubic centimeter is 35 mg. Recommended dose, 35 mg. of bismosol. The vehicle is dextrose and water containing a trace of piperazine.

after two hours. Two other injections showed a faint trace after two hours and seven days, respectively, while the remaining five injections were absorbed within periods varying from seven to fourteen days.

Bismuth Metal.—Nine patients received injections of bismuth metal suspended in isotonic dextrose solution. Two of these injections were absorbed in twenty-eight and ninety-one days, respectively. The seven other injections remained unabsorbed after seven, twenty-eight, twenty-eight, twenty-eight, forty-nine, eighty-four and ninety-one days.

SOLUTIONS OR SUSPENSIONS IN OIL

Bismuth Salicylate.—Ten patients were given injections of bismuth salicylate in oil. Five of these injections were absorbed after eleven, fourteen, twenty-eight, thirty-three and forty-two days. Two were

TABLE 2.—*Results of Injections of Thiobismol* *

Patient	Sex	Age	Number of Injections	Interval	Dose	Date of First Injection	Date of Last Injection	Date and Number of Roentgenogram	Time from Last Injection to Roentgenogram	Absorption
M. M.	F	16	4	W	1	11/21/28	12/19/28	1/21/29 A8930	33 days	Complete
M. S.	M	4	2	W	0.05 Gm.	12/ 6/28	12/20/28	12/20/28 B4262	2 hours	Complete
Mrs. H.	F	21	8	W	0.2 Gm.	.....	9/ 5/28	9/19/28 A8354	14 days	Complete
E. S.	F	9	2	W	0.075	12/ 6/28	12/20/28	12/20/28 B4261	2 hours	Complete
G. S.	F	3	1	..	0.05	.....	2/21/29	2/21/29 B4437	2 hours	Complete
D. M.	F	48	5	W	0.2 Gm.	11/21/28	12/26/28	1/ 8/29 A8864	13 days	Complete
A. M. G.	M	34	8	W	0.2 Gm.	4/19/28	5/ 3/28	5/16/28 Peters 10911	13 days	Complete

* Thiobismol, or sodium bismuth thioglycollate, is a water-soluble aqueous solution.

TABLE 3.—*Results with Injections of Bismuth Sodium Tartrate* *

Patient	Sex	Age	Number of Injections	Interval	Dose, Cc.	Date of First Injection	Date of Last Injection	Date and Number of Roentgenogram	Time from Last Injection to Roentgenogram Days	Absorption
M. Mc.	F	16	4	W	2	8/ 1/28	8/29/28	9/18/28 A8346	20	Complete
G. W.	M	40	5	W	2	8/ 1/28	9/ 5/28	9/25/28 A8287	20	Complete
R. F.	M	3 mo.	6	W	0.5	10/11/28	11/22/28	12/ 6/28 B4224	14	Complete
E. L.	M	7	6	W	1	10/25/28	12/ 6/28	12/ 6/28 B4225	2 hrs.	Complete
E. S.	F	6	5	W	1	7/26/28	8/30/28	9/ 6/28 B4023	7	Complete
M. S.	M	4	1	..	1	.....	8/16/28	9/ 6/28 B4024	21	Complete
M. C.	F	..	4	S	2	.....	8/29/28	9/13/28 A8318	15	Complete
H. H.	M	24	2	q.2 days	2	4/ 4/29	4/ 6/29	4/ 6/29	1 hr.	Complete

* For bismuth sodium tartrate, 1.5 per cent, the recommended dose is 2 cc. every two or three days. The amount of bismuth claimed per cubic centimeter is 11 mg. It is water soluble. The vehicle is aqueous solution containing 25 per cent sucrose and 25 per cent benzyl alcohol. The formula given by the manufacturer is: bismuth sodium tartrate (73.8 per cent bismuth), 0.030 Gm.; benzyl alcohol, 0.040 Gm., and sucrose, 0.500 Gm.

almost completely absorbed after twenty-eight and thirty-six days. Three others remained unabsorbed after six, twenty-one and forty-four days.

TABLE 4.—*Results of Injections of Bismarsen (Bismuth Arsphenamine Sulphonate)**

Patient	Sex	Age	Number of Injections	Interval	Dose, Gm.	Date of First Injection	Date of Last Injection	Date and Number of Roentgenogram	Time from Last Injection to Roentgenogram Days	Absorption	Comment
B. W.	F	48	10	W	0.2	1/18/28	4/11/28	5/ 5/28 A7677	24	Complete	
R. H.	M	17	10	W	...	11/25/28	2/ 3/28	2/11/28 T9504	8	Complete	Last of 10 potassium bismuth tartrate 11/18/27
G. W.	M	40	10	W	0.2	1/ 6/29	3/20/29	3/27/29 A9258	7	Complete	
L. T.	F	..	10	W	0.2	10/31/28	1/23/29	2/ 1/29 A8986	9	Complete	
W. P.	M	21	10	W	0.2	10/31/28	1/16/29	1/23/29 A8938	7	Complete	0.2 Gm. of potassium bismuth tartrate 10/17/28
M. M.	F	45	6	W	0.2	4/16/29	5/ 9/29	5/14/29 T11623	5	Complete	Very faint trace immediately after injection
G.R.M.	F	40	2	W	0.2	3/ 9/29	3/13/28	3/13/29 T11462	1 hr.	Complete	Very faint trace immediately after injection
M. M.	F	50	10	W	0.2	3/20/29	5/22/29	5/27/29 A9572	5	Complete	
G. R.	M	41	1	..	0.2	4/ 9/29	.....	5/ 9/29	30	Complete	Trace remaining after 16 days
A. M.	F	56	1	..	0.2	4/ 2/29	.....	4/21/29	22	Complete	Faint trace remaining after 7 days

* The amount of bismuth claimed per cubic centimeter is 45 mg.; in the recommended dosage, 45 mg. It is water soluble. The vehicle is distilled water containing butyn.

TABLE 5.—*Results of Injections of Bismoid**

Patient	Sex	Age	Number of Injections	Interval	Dose, Cc.	Date of First Injection	Date of Last Injection	Date and Number of Roentgenogram	Time from Last Injection to Roentgenogram Days	Absorption	Comment
Mr. R.	M	55	9	W	2	.....	9/ 6/28	9/20/28 P11118	14	Complete	
M. C.	F	Infant	2	W	0.25	4/18/29	4/25/29	5/ 9/29 B4710	14	Complete	Very faint trace after injection and 1 week
G. S.	F	3	1	..	0.25	4/11/29	4/11/29	4/18/29 B4654	7	Complete	
G. S.	F	3	1	..	0.25	.....	4/18/29	4/18/29 B4654	2 hrs.	Trace	
G. S.	F	3	1	..	0.25	.....	4/25/29	4/25/29 B4692	2 hrs.	Complete	
E. E.	F	..	1	..	1	.....	4/ 4/29	4/18/29 B4658	14	Complete	
R. F.	M	3 mo.	1	..	0.25	.....	4/ 4/29	4/11/29 B4625	7	Trace remaining	
A. A.	F	2 mo.	1	..	0.25	5/ 9/29	.....	5/16/29 B4790	7	Complete	
P. M.	M	2 yrs.	1	..	0.25	5/ 2/29	.....	5/ 2/29 B4725	2 hrs.	Complete	

* Each cubic centimeter contains 0.025 Gm. of bismuth metal; in the recommended dosage, 25 mg. It is a suspension in water solution of degradation products of dextrose.

TABLE 6.—*Results of Injections of Bismuth-Metal (Hypoloid)**

Patient	Sex	Age	Number of Injections	Interval	Dose	Date of First Injection	Date of Last Injection	Date and Number of Roentgenogram	Time from Last Injection to Roentgenogram	Absorption
E. M.	M	6 mo.	2	W	0.25 cc.	2/21/29	2/28/29	5/23/29 B4823	84 days	Small amount remaining
E. L.	M	7 yr.	8	W	0.25 cc.	12/13/28	2/ 7/29	3/ 7/29 B4492	28 days	Moderate amount remaining
B.	F	7	1	..	0.5 cc.	2/21/29	.....	2/28/29	7 days	Moderate amount remaining
J. S.	F	7	1	..	0.5 cc. left deltoid	3/21/29	.....	4/18/29 B4652	28 days	Complete
A. S.	M	5	1	..	0.5 cc. left deltoid	3/21/29	.....	4/18/29 B4653	28 days	Large amount remaining
E. M.	F	6	1	..	0.5 cc. deltoid	2/28/29	.....	3/28/29 B4575	28 days	Large amount remaining
V. P.	F	8	1	..	0.5 cc. right deltoid	2/21/29	.....	5/23/29 B4817	91 days	Faint trace remaining
M. P.	M	11	1	..	0.5 cc. right deltoid	2/21/29	.....	5/23/29 B4818	91 days	Complete
E. L.	M	7	1	..	0.5 cc.	4/25/29	.....	6/13/29	49 days	Moderate amount remaining

* * Suspended in sterile isotonic dextrose solution, 0.2 Gm. of bismuth-metal in 1 cc. The average dose for the adult is 1 cc.

TABLE 7.—*Results of Injections of Bismuth Salicylate**

Patient	Sex	Age	Number of Injections	Interval	Dose, Cc.	Date of First Injection	Date of Last Injection	Date and Number of Roentgenogram	Time from Last Injection to Roentgenogram Days	Absorption	Comment
T. H.	M	45	8	W	.....	.....	12/28/29	2/10/28 A7217	44	Small amount remaining	
V. P.	F	8	1	..	0.5	.....	5/23/29				
M. P.	M	11	1	..	0.5 (left deltoid)	.....	5/23/29				
E. E.	F	22	1	..	1	.....	5/23/29	6/13/29	21	Small amount remaining	
E. E.	M	28	1	..	1	.....	4/24/29	5/22/29 T11639	28	Complete	
C.P.H.	M	33	1	..	1	.....	3/29/29	5/ 1/29 T11601	33	Complete	
B. S.	F	40	1	..	1	.....	4/23/29	5/21/29 T11636	28	Very faint trace remaining	Large amount remaining immediately after injection
E. M.	F	42	1	..	1	.....	4/ 8/29	4/22/29 T11579	14	Complete	Moderate amount remaining immediately after injection
J. K.	M	34	1	..	1	.....	4/22/29	5/ 3/29 T11605	11	Complete	
E. L.	M	28	18	W	1	11/10/28	2/ 7/29	3/13/29 T11468	36	Faint trace remaining	
R. R.	M	..	1	..	0.13 Gm.	.....	5/22/29	5/28/29 A9575	6	Large amount remaining	
J. K.	M	28	1	..	1	.....	5/ 3/29	6/14/29 T11690	42	Complete	

* In bismuth salicylate the amount of bismuth claimed per cubic centimeter is 76.7; in the recommended dose, 76.7 mg. The vehicle is oil.

Quiniobine.—Eleven injections of quiniobine were studied. Quiniobine is an oily suspension of a soluble salt, potassium sodium bismuth tartrate, together with an insoluble salt, bismuth quinine iodide. Three injections were nearly absorbed after two hours, two and seven days, respectively. The eight remaining injections were completely absorbed

TABLE 8.—*Results of Injections of Quiniobine (Potassium Sodium Bismuth Tartrate and Bismuth Quinine Iodide)* *

Patient	Sex	Age	Number of Injections	Interval	Dose, Cc.	Date of First Injection	Date of Last Injection	Date and Number of Roentgenogram	Time from Last Injection to Roentgenogram Days	Absorption	Comment
M. C.	F	9	3	W	2	3/14/29	3/21/29	4/ 4/29 4593BH	14	Complete	Faint trace remaining at two weeks
M. C.	F	6 mo.	2	W	0.5	5/16/29	5/23/29	5/23/29 B4816	2 hrs.	Small amount remaining	
E. E.	F	22	1	..	2	5/ 2/29	.....	5/16/29 B4791	14	Complete	Roentgenogram 9 days after injection showed faint trace remaining
P. M.	M	2	1	..	0.5	5/16/29	.....	5/23/29 B4821	7	Faint trace remaining	
L.R.M	F	45	1	..	2	3/25/29	.....	4/ 9/29 T11540	15	Complete	Large amount remaining immediately after injection
B. L.	F	26	1	..	2	3/ 2/29	.....	3/16/29 T11468	14	Complete	
R. B.	F	..	1	..	2	5/15/29	.....	5/24/29 A9566	9	Complete	
R. B.	F	..	1	..	2	5/22/29	.....	5/24/29 A9566	2	Faint trace remaining	
G. K.	M	46	1	..	2	5/ 7/29	.....	5/22/29	15	Complete	
P. B.	F	21	1	..	2	5/25/29	.....	6/ 1/29 T11666	7	Complete	
M. C.	F	5 mo.	1	..	0.5	5/23/29	.....	6/ 5/29 B4816	13	Complete	

* Manufacturer claims an oily suspension, each 2 cc. of which contains bismuth, 0.030 Gm.; iodine, 0.075 Gm., and basic quinine, 0.045 Gm. It is put up in 2 cc. ampules. It is claimed to contain a water-soluble salt, potassium sodium bismuth tartrate, together with the insoluble bismuth quinine iodide.

after seven, eight, thirteen, fourteen, fourteen, fourteen, fifteen and fifteen days.

Bismogenol.—Five patients were given injections of bismogenol, an oily preparation of bismuth oxybenzoic acid. Two of these injections were absorbed after sixteen and twenty-two days. Three injections were partially absorbed after twenty-seven, twenty-eight and forty-six days.

Bismudol.—Six patients were given injections of bismudol, which is phenyl formitate of bismuth in a palmitin base. In none of these patients had the bismuth absorbed, although roentgenograms were taken after five, forty-nine, one hundred and sixty-one, one hundred and

TABLE 9.—*Results of Injections of Bismogenol* *

Patient	Sex	Age	Number of Injections	Interval	Dose, Cc.	Date of First Injection	Date of Last Injection	Date and Number of Roentgenogram	Time from Last Injection to Roentgenogram Days	Absorption	Comment
R. H.	M	16	11	W	2	3/10/28	5/23/28	7/ 8/28 T10070	46	Small amount remaining	
E. L.	M	28	1	..	2	5/ 1/29	.....	5/23/29 T11639	22	Complete	Moderate amount remaining after one week
L. C.	M	50	1	..	1	2/15/29	.....	3/14/29	27	Trace remaining	
T. S.	M	74	1	..	1	4/ 9/29	.....	4/25/29	16	Complete	
E. M.	F	42	1	..	1	5/20/29	.....	6/17/29 T11694	28	Small amount remaining	

* The amount of bismuth claimed per cubic centimeter is 60 mg.; in the recommended dose, 60 mg. The vehicle is oil.

TABLE 10.—*Results of Injections of Bismudol (Phenyl Formitate of Bismuth)* *

Patient	Sex	Age	Number of Injections	Interval	Dose, Gm.	Date of First Injection	Date of Last Injection	Date and Number of Roentgenogram	Time from Last Injection to Roentgenogram Days	Absorption	Comment
J. H.	M	13	8	W	...	7/ 4/28	2/22/28	1/30/29 A2978	161	Large amount remaining	
A. S.	M	5	5	W	0.1	5/17/28	7/12/28	1/ 3/29 B4290	175	Large amount remaining	
B. M.	F	8	6	W	1 cc.	10/18/28	12/13/28	1/31/29 B4388	48	Large amount remaining	
J. M.	F	5	18	W	0.19	.....	6/14/27	7/ 5/28 B3820	386	Large amount remaining	
J. S.	F	7	6	W	0.1	5/17/28	7/12/28	12/20/28 B4258	161	Large amount remaining	
H. H.	M	23	1	..	0.19	4/22/29	4/22/29	4/27/29 T11591	5	Small amount remaining	Large amount remaining immediately after injection

* The recommended dose is 129.5 mg., of which 70 per cent is BiO_3. The vehicle is a palmitin base.

sixty-one, one hundred and seventy-five and three hundred and eighty-six days.

Potassium Sodium Bismuth Tartrate.—Four patients were given potassium sodium bismuth tartrate in a suspension of vegetable oil and

water. Our studies on this series were interrupted and are incomplete, but two injections were unabsorbed after seven days each, one was partially absorbed after forty-two days, while the other was practically absorbed after thirty-one days.

Oleo-Bi-Roche.—Three patients were given injections of oleo-bi-Roche which is bismuth oleate in an oily vehicle. One injection was

TABLE 11.—*Results of Injections of Potassium Sodium Bismuth Tartrate with Procaine Hydrochloride* *

Patient	Sex	Age	Number of Injections	Dose, Cc.	Date of First Injection	Date and Number of Roentgenogram	Time from Last Injection to Roentgenogram, Days	Absorption
M. A.	F	9	1	1.0	5/16/29	5/23/29 4820B	7	Moderate amount remaining
R. S.	M	8 mo.	2	0.5	5/16/29	5/23/29 B4819	7	Large amount remaining
B. L.	F	26	1	1.0	2/13/29	3/16/29 T11468	31	Very faint trace remaining
E. M.	M	9 mo.	1	0.5	5/ 2/29	6/13/29 B4913	42	Moderate amount remaining

* Manufacturer's claim: Each cubic centimeter contains potassium sodium bismuth tartrate, 0.2 Gm.; procaine hydrochloride 1 per cent suspended in vegetable oil. The amount of bismuth claimed per cubic centimeter is 64.3; in the recommended dosage, 128.6. It is water soluble; the vehicle is vegetable oil and distilled water.

TABLE 12.—*Results of Injections of Oleo-Bi* *

Patient	Sex	Age	Number of Injections	Interval	Dose	Date of First Injection	Date of Last Injection	Date and Number of Roentgenogram	Time from Last Injection to Roentgenogram	Absorption
J. K.	M	8	5	W	0.666 cc.	9/ 6/28	10/25/28	11/15/28 B4183	31 days	Complete
M. K.	F	9	4	W	0.666 cc.	9/13/28	10/25/28	3/ 7/29 B4488	133 days	Moderate amount remaining
L. K.	F	6	4	W	0.666 cc.	9/13/28	10/25/28	3/14/29 B4525	133 days	Small amount remaining

* In this substance the vehicle is oil.

absorbed after twenty-one days, but two others remained unabsorbed after one hundred and thirty-three days.

Iodobismuthate of Quinine.—Two patients were given injections of iodobismuthate of quinine. These injections were completely absorbed in twenty-six and forty days.

Endobismuth.—Three patients were given injections of endobismuth. We were not able to ascertain the composition of this product, but from its appearance one would believe that it was similar to iodobismuthate

of quinine. All three injections were completely absorbed in one, four and seven days, respectively.

X-Iodo-Bi.—Four patients were given injections of x-iodo-bismuth, the composition of which we could not ascertain. One injection was

TABLE 13.—*Results of Injections of Iodobismuthate of Quinine*

Patient	Sex	Age	Number of Injections	Interval	Dose, Cc.	Date of First Injection	Date of Last Injection	Date and Number of Roentgenogram	Time from Last Injection to Roentgenogram Days	Absorption	Comment
Mr. E.	M	39	1	..	5	5/ 3/28	.....	5/29/28 10935 (Peters)	26	Complete	
Mr. F.	M	44	2	W	5	6/ 1/28	6/ 8/28	7/28/28 11014 (Peters)	40	Complete	Large amount remaining immediately after injection

TABLE 14.—*Results of Injections of Endobismuth* *

Patient	Sex	Age	Number of Injections	Interval	Dose, Cc.	Date of First Injection	Date of Last Injection	Date and Number of Roentgenogram	Time from Last Injection to Roentgenogram Days	Absorption	Comment
Mrs. E.	F	39	1	..	4	4/24/29	.....	5/ 1/29 T11600	7	Complete	Large amount remaining immediately after injection
Mr. K.	M	34	1	..	4	5/ 9/29	.....	5/13/29 T11616	4	Complete	Large amount remaining immediately after injection
Mr. H.	M	24	1	..	4	4/11/29	.....	4/12/29 T11553	1	Complete	

* In this substance the vehicle is an oil.

TABLE 15.—*Results of Injections of X-Iodo-Bismuth* *

Patient	Sex	Age	Number of Injections	Dose, Cc.	Date of First Injection	Date and Number of Roentgenogram	Time from Last Injection to Roentgenogram, Days	Absorption
M. A.	F	..	1	2	5/ 8/29	6/ 5/29 A9594	28	Large amount remaining
T. L.	F	25	1	1	5/ 8/29	5/29/29	21	Small amount remaining
L. S.	F	40	1	2	5/ 8/29	5/24/29	16	Large amount remaining
J. H.	M	12	1	1	5/ 8/29	5/16/29	8	Complete

* One cubic centimeter contains 17 cg. of x-iodo-bismuth in a neutral, sterile, oily suspension. The dose is 2 cc. intramuscularly. The amount of bismuth claimed per cubic centimeter is 28.6 mg.; in the recommended dosage, 47.2 mg.

completely absorbed in eight days. Three others showed little absorption after sixteen, twenty-one and twenty-eight days, but could not be followed longer.

Potassium Bismuth Tartrate.—Twenty injections of potassium bismuth tartrate in oil suspension were studied. Sixteen of these injec-

tions were absorbed completely in periods varying from twelve to one hundred and twenty-seven days. Four other injections were almost entirely absorbed after thirteen, fourteen, twenty-one and thirty-six days.

TABLE 16.—*Results of Injections of Potassium Bismuth Tartrate with Butyn* **

Patient	Sex	Age	Number of Injections	Interval	Dose	Date of First Injection	Date of Last Injection	Date and Number of Roentgenogram	Time from Last Injection to Roentgenogram	Absorption
H. C.	F	35	38	W	0.2 Gm.	6/22/26	7/18/28	8/ 8/28 A8162	21 days	Faint trace remaining
D. M.	F	48	10	W	0.2 Gm.	1/30/29	2/ 6/29	3/14/29	35 days	Faint trace remaining
M. G.	M	58	20	W	0.2 Gm.	2/20/28	10/31/28	3/ 7/29 A9259	127 days	Complete
M. H.	F	21	9	W	0.2 Gm.	1/16/29	3/13/29	3/26/29	13 days	Small amount remaining
M. Mc.	F	16	5	W	0.1 Gm.	1/30/29	2/27/29	3/13/29 A9166	14 days	Faint trace remaining
M. Mc.	F	16	1	..	0.1 Gm.	1/ 9/29	.....	1/21/29 A8930	12 days	Complete
W. P.	M	21	1	..	0.2 Gm.	10/17/28	.....	1/23/29 A8938	108 days	Complete
H. C.	F	35	Many	W	0.2 Gm.	.....	12/ 5/28	1/15/29 A8897	41 days	Complete
G. W.	M	40	10	W	0.2 Gm.	10/ 3/28	12/12/28	1/15/29 A8896	34 days	Complete
R. B.	F	21	12	W	0.2 Gm.	1/ 4/28	3/28/28	5/18/28 A7775	51 days	Complete
E. M.	F	6	10	W	0.1 Gm.	.....	9/ 8/27	1/12/28 B3304	126 days	Complete
B.	..	..	2	W	0.1 Gm.	12/ 6/28	1/24/29	1/24/29 B4359	.....	Complete
J. S.	F	6	8	W	0.1 Gm.	12/ 1/27	2/16/28	4/13/28 B3556	56 days	Complete
E. S.	F	4	4	W	0.1 Gm.	9/ 6/28	9/27/28	12/20/28 B4261	84 days	Complete
M. K.	F	9	2	W	0.1 Gm.	2/ 9/28	3/ 1/28	3/30/28 B3506	29 days	Complete
L. K.	F	6	16	W	0.05 Gm.	4/15/27	3/ 1/28	3/29/28 B3505	28 days	Complete
R. F.	M	3 mo.	5	W	0.05 Gm.	12/ 6/28	2/ 7/29	2/28/29 B4461	21 days	Complete
F. C.	M	12	22	W	0.1 Gm.	4/25/28	11/28/28	1/15/29 A8898	48 days	Complete
K. J.	M	8	11	W	0.1 Gm.	6/10/27	3/ 1/28	3/30/28 B3504	29 days	Complete
L. B.	F	45	1	..	0.2 Gm.	4/ 9/29	.....	6/12/29	64 days	Complete

* The manufacturer claims that each ampule contains 2 cc.—potassium bismuth tartrate, 0.2 Gm., and butyn, 0.6 per cent, in oil suspension. It is put up in 2 cc. ampules. The dose (maximum) is 2 cc. (67 mg. of bismuth). The amount of bismuth claimed per cubic centimeter is 33.5 mg. It is water soluble. The substance is suspended in oil of almonds and olive oil.

Mesurol.—Twelve injections of mesurol were studied. This is an oily suspension of the basic bismuth salt of dioxybenzoic acid methyl ether. None of these injections was absorbed in fifteen, seventeen, twenty-one, twenty-eight, twenty-eight, twenty-eight, forty-three, forty-nine, seventy-seven, ninety-six, one hundred and ten and one hundred and thirteen days.

REPORT OF STUDIES ON RABBITS

Each of fifteen rabbits of approximately the same weight and age received an injection of a bismuth compound into the gluteal muscles. Fifteen different compounds of bismuth were used. The doses given to rabbits were one eighth of the dose recommended for an adult patient. These relatively large doses were given because we feared that there would be little roentgen visualization of the small doses proper for a

TABLE 17.—*Results of Injections of Mesurol* *

Patient	Sex	Age	Number of Injections	Interval	Dose	Date of First Injection	Date of Last Injection	Date and Number of Roentgenogram	Time from Last Injection to Roentgenogram	Absorption
N. K.	F	30	9	W	1 cc.	10/31/28	12/26/28	4/ 1/29 A9293	96 days	Small amount remaining
N. K.	F	60	9	..	.....	10/31/28	12/26/28	3/13/29 A9168	77 days	Small amount remaining
M. C.	F	40	10	W	1 cc.	10/17/28	12/19/28	1/ 3/29 A8845	15 days	Large amount remaining (both hips)
B. W.	F	45	5	W	1 cc.	10/24/28	12/26/28	4/15/29 A9185	110 days	Large amount remaining
M. K.	F	9	4	W	0.5 cc.	5/24/28	6/28/28	7/26/28 B3877	28 days	Faint trace remaining
J. K.	M	8	3	W	0.5 cc.	5/24/28	6/28/28	7/26/28 B	28 days	Faint trace remaining
E. M.	F	6	7	W	.....	.....	7/ 5/28	7/26/28 B3876	21 days	Moderate amount remaining
B. L.	F	26	1	..	1 cc.	3/30/29	.....	5/18/29 T11626	49 days	Small amount remaining
J. L.	F	25	1	..	1 cc.	3/13/29	.....	4/25/29 T11536	43 days	Small amount remaining
J. G.	F	30	1	..	1 cc.	3/19/29	.....	4/16/29	28 days	Small amount remaining
G. A.	M	56	1	..	1 cc.	4/ 3/29	.....	4/20/29	17 days	Faint trace remaining
J. S.	F	41	1	..	1 cc.	2/19/29	.....	6/12/29	113 days	Large amount remaining

* In mesurol, or basic bismuth salt of dioxybenzoic acid methyl ether, the amount of bismuth in each cubic centimeter is 110 mg., in the recommended dosage, 110 mg. It is insoluble in water. The vehicle is sesame oil.

rabbit's weight. The roentgenograms of the rabbits were made shortly after the injections and then at weekly intervals until no shadow of bismuth could be seen.

CONSIDERATION OF RESULTS OF ABSORPTION RATE IN EXPERIMENTAL ANIMALS

It is important to note that the absorption rate of some of the products in our animals differed markedly from the absorption rate of the same products in patients. We cannot explain these discrepancies

TABLE 18.—*Results of Injections of Bismuth Compounds into Rabbits*

Water-Soluble Compounds. Time Interval from Injection to Roentgenogram

Rabbit	Brand	Day	1 Week	2 Wks.	3 Wks.	4 Wks.	5 Wks.	6 Wks.	7 Wks.	8 Wks.	9 Wks.	10 Wks.	11 Wks.	12 Wks.	13 Wks.	14 Wks.	15 Wks.	
1	Thiobismol	Same +	0	..	0	..	..	..	0	..	..	..	..	..	..	..	..	.....
2	Sodium bismuth tartrate	3d ++	++	++	++	+	..	0	..	..	..	0	..	..	..	..	..	.....
3	Potassium sodium bismuth tartrate	Same 0	0	0	..	.	..	..	..	..	..	..	..	..	..	..	..	.....
4	Bismuth arsphenamine sulphonate	3d +++	+++	+++	++	++	..	+	..	..	0	..	..	..	..	..	..	.....
							Suspensions											
5	Bismuth metal	Same ++++	..	..	++++	..	..	++++	..	..	+++	..	+++	..	..	+++	..	After 22 weeks still +++
6	Bismuth in dextrose	3d ++++	+++	+++	++	+	..	+	..	..	..	+	..	..	0	..	..	.....
							Solutions or Suspensions in Oil											
7	Basic bismuth methoxy hydroxy benzoate	4th ++++	+++	++	..	+	..	..	+	..	..	+	..	..	..	..	+	.....
8	Phenyl formitate of bismuth	3d ++++	+++	++	++	+	..	+	..	..	..	..	..	..	0	..	..	.....
9	Potassium bismuth tartrate	3d +++	+++	+++	+++	++	..	+	..	..	..	+	..	..	0	..	..	.....
10	Bismuth oxybenzoic acid	3d +++	++	++	++	++	..	+	..	..	..	0	..	..	..	..	..	.....
11	Bismuth quinine iodide and potassium sodium bismuth tartrate	Same ++++	+	+	..	0	..	..	..	..	..	.	..	..	..	..	..	.....
12	Potassium sodium bismuth tartrate	Same ++++	+++	..	..	..	+	..	..	..	..	..	..	..	..	..	..	.....
13	Iodobismuthate of quinine	3d 0	0	0	0	0	..	..	..	..	..	..	..	..	..	..	..	.....
14	Bismuth oleate	3d ++++	+++	+++	++	++	..	++	..	..	..	+	..	..	..	0	..	.....
15	Bismuth salicylate	Same ++++	++++	++++	++++	++++	..	+++	..	..	..	+++	..	..	+++	..	..	After 29 weeks still +++

at present. It is possible that the tissue juices have a different chemical reaction toward the bismuth salts used, thus varying the absorption rate.

This difference is strikingly illustrated in the soluble salt sodium bismuth tartrate (rabbit 2) which required six weeks for total absorption, whereas in none of our eight patients who received it did it require more than twenty days to absorb, generally absorbing within a few hours. The same holds true for bismuth arsphenamine sulphonate (rabbit 4) which was completely absorbed only after ten weeks. In man it was always completely absorbed within thirty days, and generally within a few hours.

One of the suspensions, bismoid, required thirteen weeks for total absorption in rabbit 6, while in all of our patients it had disappeared within fourteen days.

The absorption rate of the oily suspensions and solutions in rabbits more nearly paralleled the results found in patients. Most of our patients absorbed bismuth salicylate within five weeks, but in rabbit 15 little evidence of absorption could be found even after twenty-nine weeks.

From the practical standpoint, then, we believe that our results here are of far less value than the results of our similar studies in patients and that future roentgenologic studies of the absorption rate of bismuth should be made on the actual patient rather than on rabbits.

Some investigators have criticized the roentgenologic method of determining the rate of absorption of bismuth. Gruhzit and his co-workers [6] used a method dependent on the destruction of the experimental animals at varying lengths of time following the injection and the determination of the amount of bismuth remaining in the muscle by means of chemical analysis. This is undoubtedly the most accurate method that could be devised but it is not applicable to patients. They have also determined the amount of bismuth excreted in the urine and feces. This method gives no information as to whether the bismuth which has not been excreted has remained at the site of the injection or whether it has been stored elsewhere in the body. Another worker killed his animals at stated intervals and perfused their vessels with a sulphide solution. The black precipitate which formed at the point of contact of sulphide with bismuth indicated the presence of unabsorbed bismuth. This, again, is not applicable to man.

The weightiest evidence against our method is that of Gruhzit.[7] He stated that after the roentgen ray had demonstrated complete absorption

6. Gruhzit, O. M.; Tendick, F. H., and Sultzaberger, J. A.: Bismuth Absorption, Distribution and Elimination, Am. J. Syph. **21**:87, 1927.

7. Gruhzit, O. M., discussion on Cole, Farmer and Miskdjian (footnote 3, p. 228).

of the bismuth, considerable amounts could be recovered at the site of injection. Gruhzit and his co-workers [6] stated that the time necessary for apparent absorption may be unduly prolonged by shadows cast by calcium soap deposits formed by the oils used as vehicles for the insoluble bismuth preparations. We believe that this objection is largely a theoretical one. Gruhzit [5] also claimed that potassium bismuth tartrate and bismuth oleate cast no shadows because of muscle necrosis occurring around the injections and obscuring them. We have not been able to see how a soft tissue necrosis could possibly obscure the shadow cast by a salt of a heavy metal.

All of these supposedly more accurate methods depend on experiments on animals. Let it be granted that more accurate data may be obtained by animal experimentation. Of how much value is it? Our work on animals would indicate that the absorption rate of some bismuth products is not the same in rabbits as in patients. Hence, we feel that the method we have followed is a better index of the absorption rate in man, as well as more practical.

We have been interested solely in the absorption rate of the various bismuths and have not attempted to study their therapeutic value. In our present state of knowledge we may have opinions as to how rapidly a bismuth salt should be absorbed, but we have little proof as to whether or not the extremely rapidly absorbed soluble salts are superior to the more slowly absorbed insoluble salts in oil. Some authors have maintained that the establishment of a depot of slowly absorbing bismuth is desirable while others desire a product which is absorbed rapidly and which, theoretically at least, floods the system with a large amount of bismuth in a short time.

SUMMARY

Studies have been made of the absorption rate of seventeen different brands of bismuth in man. The absorption rate of fifteen of these brands has also been determined in the experimental animal (rabbit).

Our results in rabbits are so at variance with our results in patients as to lead us to believe that future similar studies should be on patients, not on rabbits.

COMMENT

We are content at present merely to submit our observations without attempting to deduce therapeutic recommendations There is undoubtedly much need of further investigation with a view to the correlation of clinical observations, serologic tests and roentgenologic records together with dosage and chemical and physical characteristics of the brand of bismuth used. The patient himself must also be considered as to duration of the disease, previous treatment, age, sex, etc. It is

only as we are able to collect sufficient data with as many of these factors reduced to comparative values that our conclusion will be of definite value.

ABSTRACT OF DISCUSSION

DR. COLE, Cleveland: One thing that impressed us all as we listened to Dr. Templeton's paper is the fact that although we have used bismuth for only a few years there are already many different bismuth preparations on the market. We cannot blame the man in general practice who is treating patients for syphilis when he becomes confused as to which is the best preparation to use. With mercury enough work has been done so that we have selected a few preparations that will do certain things and we can employ them for certain purposes, but with bismuth we have a mass of preparations that we know little about except what the manufacturer tells us, and any work which tends to check up what these things will do is of value. When we find a preparation in the list which is not absorbed for three hundred and sixty-six days, that probably is of little value for the patient and it is well to keep it out of the list. If others in the list are found not to absorb readily, such as the oleates, they also should be eliminated. What is the man in general practice to do? Probably follow the suggestions of the Council on Pharmacy and Chemistry of the American Medical Association. This is not entirely worked out but it is probably the best advice we have at the time.

I do not agree with Dr. Templeton when he says that the study of the elimination will not help us, for I think that it is of great value. It will give us definite information as to the rate of absorption.

Regarding soap deposits in injections of bismuth, the work was not original with Dr. Gruhzit. It was brought out by the French school some years ago.

DR. NORMAN N. EPSTEIN, San Francisco: The essayist has emphasized the difficulty we have in selecting bismuth compounds with which to treat our patients in clinic and office practice. Watching the patient carefully will tell whether the bismuth compound used is active therapeutically. We used bismudol at one time quite extensively, but we failed to get the bismuth line on the gum with any amount that was given. I think that we must select a compound that is active and use it until some one gives us a better one. We watched a few patients with positive dark-field tests under bismudol, but failed to get a negative dark field; so we changed to bismuth potassium tartrate and got a negative dark-field examination within a short time. Some of the lesions actually increased in size under bismudol. A preparation that will control syphilitic lesions and will give evidences of absorption of bismuth, such as headache, weakness, joint pains and so forth, should make us feel confident that we are getting a bismuth result.

DR. SULZBERGER, New York: I agree with Dr. Templeton that one cannot judge the therapeutic efficacy of a preparation by the speed with which it disappears from the point of injection. I wish to ask Dr. Templeton whether he noticed any connection between the speed with which a drug disappears from the site of injection and the appearance of pain and other disagreeable symptoms. During eight years in Europe studying medicine, three of which were spent in dermatology and syphilis, I did not see an injection or an inunction of mercury given in the treatment for syphilis. In the clinics in which I worked mercury has been practically entirely replaced by bismuth. In the clinic in Zurich we used a preparation of bismuth and were well satisfied with it. There was sufficient evidence that the bismuth was being resorbed. Some patients showed a

stomatitis of slight degree, and there were also some patients with secondary syphilids, who showed a marked Herxheimer reaction after the first injection of this bismuth compound.

Dr. Templeton, Oakland, Calif.: In reply to Dr. Sulzberger's question, I have tried to remember the relation of pain to the rate of absorption, but I do not think that I can correlate the two. Some of the rapidly absorbed water-soluble compounds were absolutely painless and some caused pain. With the oily suspensions, I can think of one that caused considerable pain and yet it was to my mind one that was absorbed at the optimum time. I think that one cannot judge absorption rate according to the pain.

THE OCCURRENCE OF FUNGI IN PATIENTS WITH MALIGNANT DISEASE *

J. ARTHUR BUCHANAN, M.D.

BROOKLYN

The relationship of fungi or yeasts to carcinomas and other types of malignant tumors has been considered many times.[1]

The source of continued contamination in patients with well recognized cutaneous manifestations due to fungi has been a point of considerable interest.[2] During the last several years, I have cultured the gastric contents and stools of these patients for fungi. In practically all instances the cultures were positive. During the past year, because of frequent symptoms and at times physical observations in the mouths of many of the patients, the saliva was cultured.[3] A correlation of the observations on the saliva and gastric contents and the stools showed that if the saliva were positive, the remainder of the gastrointestinal tract was usually positive. In patients with slight disturbance the saliva was negative, while the cultures of the gastric contents and stools were usually positive. The results of the studies indicated that the source of continued contamination was in the intestinal tract. The details of the work will be reported in the near future.

Many of the different strains of fungi were studied in more or less detail on various types of solutions of sugar. The testing of these solutions, by the bichromate test, for alcohols and other products of yeast metabolism stimulated me to examine the urine and saliva of the patients for similar products.[4] The tests gave positive reactions in all instances.

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* Submitted for publication, Oct. 18, 1929.

1. Williams, W. Roger: The Natural History of Cancer, New York, William Wood & Company, 1908, pp. 249-262. Castellani, Aldo: Fungi and Fungous Diseases, Arch. Dermat. & Syph. **17**:61, Jan.; 194, Feb.; 354, March, 1928. Guilliermond, Alexandre: The Yeasts, New York, John Wiley & Sons, 1920, p. 349. Ewing, James: Neoplastic Diseases, Philadelphia, W. B. Saunders Company, 1928, p. 127.

2. White, C. J.: Fungus Diseases of the Skin, Arch. Dermat. & Syph. **15**: 387 (April) 1927. Weidman, Fred D.: Laboratory Aspects of Epidermophytosis, Arch. Dermat. & Syph. **15**:415 (April) 1927.

3. Zeisler, E. P.: Monilia Infection of the Tongue, Arch. Dermat. & Syph. **15**:171 (Feb.) 1927.

4. Richter: Organic Chemistry, Philadelphia, P. Blakiston's Son & Company, 1919, vol. 1, p. 199. McCollum, E. V.: A Text-book of Organic Chemistry, New York, The Macmillan Company, 1923, p. 55. Steel, Matthew: Manual of Organic Chemistry, New York, John Wiley & Sons, 1920, p. 32.

In an endeavor to ascertain whether malignant growths were a particular type of expression of fungal metabolism and to add further information to the observations of others that the growths were of mycotic origin, the following investigations were made to determine whether the saliva of the patients with malignant disease would yield the same results as that from patients with benign cutaneous lesions caused by fungi. The clinical diagnosis in each patient was confirmed by microscopic examination of tissue. The specimens of saliva were obtained from patients in the Brooklyn Cancer Institute and from my private patients. I collected the salivas in sterile bottles while the patient was being observed.

The cultures were made on Sabouraud's mediums for yeasts and on beerwort agar. They were incubated at 37.5 C. for twenty-four hours. In some instances cultures were made from the diseased areas, but they are not reported, as there is no way of excluding air contamination. The latter criterion applies to the cultures made from cutaneous lesions caused by fungi.

The bichromate test was done on all specimens of urine and saliva. The method consisted in using 2 cc. of urine in a graduated centrifuge tube, to which was added 0.5 cc. of 10 per cent potassium bichromate. Concentrated sulphuric acid was then added, drop by drop, until the solution was entirely green. The figure recorded as the end-point was in reverse relationship to the quantity of products of yeast metabolism present. The test on the saliva was qualitative. A few drops of bichromate solution were added to a small quantity of saliva. The sulphuric acid was added drop by drop until the end-point was reached.

The iodoform test for alcohol and other products of yeast metabolism may be performed on the urine and saliva.[5] The same quantity of urine may be used, while compound solution of iodine and 40 per cent sodium hydroxide are substituted in the same amounts for the chemicals used for the bichromate test. The final color reaction is yellow. The crystals of iodoform may be examined under the microscope when the odor of iodoform is not distinctive. The end-points run parallel to those of the bichromate test, but the reaction is not so clearly cut as in the latter test.

The tests both gave negative results in normal urine and saliva.[6] However, any one who investigates the subject must do considerable work before arriving at that conclusion.

The colonies were white in all instances unless otherwise specified in the tables. The patient in case 2910 was clinically cured at the time

5. Guilliermond (footnote 1, third reference, p. 163).

6. Buchanan, J. A.: Urine Tests for Some of the Products of Yeast Metabolism, South Med. & Surg. **91**:390 (June) 1929.

of the examination. She had been treated by roentgen therapy. The urine test showed active fermentation going on in the stomach and the intestine. In case 2800, the patient had a fungus involvement of the nails of the left hand, a condition which had been present for many years.

TABLE 1.—*Results of Cultures and of the Bichromate Test in Cases of Carcinoma*

Case	Site of Carcinoma	Culture of Saliva	Bichromate Test	
			Saliva	Urine
2173	Breast	Profuse growth	Positive	1.0
3443	Breast	Profuse growth	Positive	0.6
3203	Breast	Profuse growth	Positive	1.2
3255	Breast	Several colonies	Positive	0.8
3161	Breast	Several colonies	Positive	0.6
T. S.	Breast	Profuse growth	Positive	0.6
H. W.	Breast	Profuse growth	Positive	1.0
O. M.	Breast	Profuse growth	Positive	1.1
3384	Cervix	Profuse growth of yellowish colonies	Positive	0.8
3022	Cervix	Profuse growth	Positive	0.8
2900	Cervix	Few colonies	Positive	1.2
2877	Cervix	Several colonies	Positive	0.8
2489	Cervix	Several colonies	Positive	1.0
3150	Uterus	Profuse growth	Positive	0.8
2907	Uterus	Negative	Positive	1.0
2988	Uterus	Several small pink colonies	Trace	0.9
2910	Uterus	Negative	Positive	0.4
3016	Uterus	Several colonies	Positive	0.8
E. E.	Uterus	Profuse growth	Positive	0.7
L. S.	Uterus	Profuse growth	Positive	0.6
3556	Urethra	Profuse growth	Trace	1.0
2640	Lip	Several colonies	Positive	0.6
2419	Mucous membrane, lower jaw	Profuse growth	Positive	1.0
837	Mucous membrane, lower jaw	Several brown colonies	Positive	0.9
2950	Mucous membrane, lower jaw	Profuse growth	Positive	0.8
1007	Tonsil	Several colonies	Positive	0.8
630	Stomach	Profuse growth	Positive	0.4
2552	Stomach	Profuse growth	Positive	1.4
1963	Stomach	Many small yellow colonies	Positive	1.2
2876	Stomach	Several colonies	Positive	0.8
B. B.	Stomach	Profuse growth	Positive	0.8
J. H.	Stomach	Profuse growth	Positive	0.6
2815	Colon	Profuse growth	Positive	1.5
R. S.	Colon	Several colonies	Positive	0.6
S. S.	Colon	Profuse growth	Positive	1.4
5081	Rectum	Profuse growth	Positive	0.6
3309	Rectum	Several colonies	Positive	1.0
4778	Rectum	Profuse creamy growth	Positive	0.6
2961	Ovary	Profuse growth	Positive	0.8
1833	Skin of forehead	Few colonies	Positive	0.4
3187	Skin of face	Profuse growth	Positive	1.6
1215	Skin of neck	Profuse growth	Positive	1.6
2579	Skin of neck	Profuse growth	Positive	4.0
339	Eyelid	Profuse growth	Positive	1.0
R. F.	Gallbladder	Profuse growth	Positive	0.9

TABLE 2.—*Results of Cultures and of the Bichromate Test in Cases of Carcinoma*

Case	Site of Sarcoma	Culture of Saliva	Bichromate Test	
			Saliva	Urine
1473	Breast	Profuse growth	Positive	0.4
2596	Foot	Profuse growth	Positive	1.0
2846	Nose	Profuse growth	Positive	1.0
2800	Thigh	Profuse growth	Positive	1.3
2924	Testicle	Profuse growth	Positive	1.0

As practically all solutions in which fungi are active become acid in reaction, the saliva of twenty-seven patients was tested. It was strongly acid to the litmus test in twenty-two patients with carcinoma and slightly alkaline or neutral in three patients who were in good clinical condition. In two patients with advanced disease, the tongues were so dry that the test could not be made.

An analysis of tables 1 and 2 shows that the saliva of forty-eight of the patients with malignant disease was positive for fungi. It is practically impossible to classify the different types by name. In only two instances was the saliva negative for fungi. The urine and saliva in all instances gave a positive reaction to the bichromate test. The test is not indicative of malignant disease, but shows fermentative processes going on in the stomach and the intestine of the patient, either as a specific expression or as an associated phenomenon.

The clinical significance of a positive reaction to the bichromate test in the urine cannot be understood until a group of patients with benign cutaneous lesions due to fungi is observed while under a special dietary and therapy regimen.[7]

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7. Buchanan, J. A.: The Dietetic Treatment of Fungous Diseases, South Med. & Surg. **92**:166 (March) 1930.

A LIST OF CUTANEOUS IRRITANTS *

LEONARD F. WEBER, M.D.
CHICAGO

This list of irritants is the outgrowth of memoranda which I have accumulated ever since I became associated with Dr. William Allen Pusey, who, at the start, impressed me with the importance of irritants in the production of dermatitis and eczema and suggested then the compilation of the list. This list includes all cutaneous irritants which so far as I have been able to discover are reported in the literature. Many proprietary cosmetics and other proprietary substances are included. This is not in itself sufficient to condemn them any more than it is sufficient to condemn a flower, for example; for some substances so rarely produce irritation that the practical advantage of their use offsets the disadvantage of the rare chance of a dermatitis.

The more one sees of inflammatory dermatoses, the more one is likely to be impressed with the importance of external irritants in their production and the necessity for using all one's ingenuity in tracing them, and yet there is no full list of them readily available. This list [1] has been useful in refreshing the mind on possible sources of irritation when searching for irritants in suspected cases. It is also useful in impressing patients with the importance of irritants and gaining their cooperation in discovering them.

HAIR DYES AND HAIR TONICS

Hair Dyes
- Barbo Comp
- "Black Dye"
- Brownatone
- Kolor-Bak
- Lux—imported
- Perfecto
- Rapidol

* Submitted for publication, Jan. 8, 1930.

* This article is intentionally confined to a list of irritants, in order to avoid overloading it and causing confusion as to its purpose. Other information concerning dermatitis from irritants is easily obtainable.

* Anyone working on this subject will find Prosser White's work on industrial dermatoses the invaluable reference book. Further references are given, but particular mention should be made of the following: White, R. Prosser: The Dermatoses or Occupational Affections of the Skin, ed. 3, London, H. K. Lewis & Company, 1928. White, James C.: Dermatitis Venenata, Boston, Cupples & Hurd, 1887. Cole, Harold N.: Investigation of Injuries from Hair Dyes, Dyed Furs and Cosmetics, J. A. M. A. **88**:397 (Feb. 5) 1927.

1. Because of the desirability of such a list for reference by dermatologists and those interested in occupational diseases, this list will be produced in pamphlet form for ready reference, and can be obtained by addressing the American Medical Association, 535 North Dearborn Street, Chicago.

Hair Dyes and Hair Tonics—*Continued*

"Despotts"
Eau Sublime
Golden Glint
Henna
Inecto
Wyeth's Sage and Sulphur
Youth-O-Lede
Inecto Rapid No Tox
False Hair Dye [2]

Hair Tonics

Auxiliator (Westphal's)
Danderine
Farr's
"Hair Vim"
Herpicide
K.D.X.
Liquid Arvon
Lucky Tiger
Mahdeen
Mascara
Quinine
Quinine Resorcin
Wildroot
Hair Restorer
Henna (Shampoo)

COSMETICS

Bleaches

Freckle Bleach
Harriet Hubbard Ayers Bleach
Lemon Cream Bleach
Face Bleach

Creams

"Freckle Cream"
Stillman's Freckle Cream
Harriet Hubbard Freckle Cream
Pompeian Night Cream
Lemon and Glycerine Cream
Lemon Cream
Harriet Hubbard Cold Cream

Powder

"Face Powder"
Talcum Powder
Armon's Powder
Hudnut's Liquid Violet Talcum
Aeolian Rouge Face Powder

Rouge

"Rouge"
Lipstick
Lipstick (Armon's)

Miscellaneous

Black and White Ointment
Mercolized Wax
"Marcirillo"
Slendaform Flesh Reducer
Grease Paint
Elmo

MISCELLANEOUS SUBSTANCES

Benetol
"Deodorant"
Depilatory
Hair Mode
Mouth Wash
Neet
Odorono
Orris Root
"Perfume"
Soap (Germicidal)
Stacomb
Toilet Water
Toilet Water (Golden Glint)
Toilet Water (Lilac)

IRRITATING PLANTS OF THE UNITED STATES [3]

Scientific Name	Common Name
Abies excelsa	Norway spruce
Aconitum napellus	Aconite
Actaea alba (L) Mill	White baneberry

2. Goldstein, M. B.: Dermatitis Venenata from Hair Dye in False Hair, J. A. M. A. **190**:1584 (May 12) 1928.

3. Made up chiefly from list of irritating plants in the United States (March, 1923) furnished Dr. William Allen Pusey by the Bureau of Plant Industry of the Department of Agriculture.

Scientific Name	Common Name
Actaea spicata	Baneberry
Agave americana	Century plant
Ailanthus glandulosa	Tree of heaven
Alismo plantago	Water-plantain
Allium sativum	Garlic
Ambrosia artemisiifolia	Common ragweed
Ambrosia psilostachya	Western ragweed
Anemone patens	Pasque flower
Anemone quinquefolia L.	Wood anemone
Anthemis cotula L.	Dog fennel
Aralia spinosa L.	Southern prickly heat
Arctium lappa L.	Burdock
Arisaema triphyllum (L) Schott	Indian turnip
Asparagus officinalis L.	Asparagus
Bidens frondosa L.	Beggar ticks
Borago officinalis L.	Borage
Brassica alba (L) Boiss	White mustard
Brassica nigra (L) Koch	Black mustard
Buxus sempervirens L.	Box tree
Cactus grandiflorus	Night-blooming cereus
Capsicum fastigiatum	Red pepper
Catalpa catalpa (L) Karst	Catalpa tree
Caulophyllum thalictroides (L) Michx	Blue cohosh
Ceanothus velutinus Dougl	Sticky laurel
Artemisia heterophylla Nutall	California mugwort
Chelidonium majus	Celandine
Chimaphila umbellata (L) Nutt	Pipsissewa
Chysanthemum leucanthemum L.	Ox-eye daisy
Chysanthemum Parthenium (L) Pers	Feverfew
Clematis virginica L.	Virgin's bower
Colchicum autumnale L.	Meadow saffron
Convallaria majalis L.	Lily of the valley
Cypripedium hirsutum Mill	Yellow ladies' slipper
Cypripedium parviflorum Salisb	Small yellow ladies' slipper
Cypripedium reginae Walt	Showy ladies' slipper
Daphne mezereum L.	Mezerum
Datura stramonium	Jamestown weed
Daucus carota L.	Wild carrot
Dirca palustris L.	Leather-wood
Drosera rotundifolia L.	Sundew
Echium vulgare L.	Viper's bugloss
Erigeron canadensis L.	Butter-weed
Euphorbia antisyphilitica Zucc	Candelilla
Euphorbia corollata L.	Flowering spurge
Euphorbia cyparissias L.	Cyprus spurge
Euphorbia helioscopia L.	Wart weed
Euphorbia ipecacuanhae L.	Ipecac spurge
Euphorbia lathyrus L.	Caper spurge
Euphorbia marginata Pursh	Snow on the mountain
Fagopyrum fagopyrum (L) Karst	Buckwheat
Fiscus carica L.	Fig

Scientific Name	Common Name
Gelsemium sempervirens (L) Ait. f.	Yellow jessamine
Ginkgo biloba L.	Ginkgo tree
Hedra helix L.	Ivy
Helenium autumnale L.	Sneezewood
Helianthus annuus L.	Sunflower
Heracleum lanatum Michx.	Cow parsnip
Hibiscus esculentus L.	Okra
Hippomane Mancinel la L.	Manchineel
Humulus lupulus L.	Hop
Iris florentina L.	Orris root
Iva xanthifolia Nutt.	Marsh elder
Juniperus virginiana L.	Red cedar
Laportea canadensis.	Wood nettle
Lepidium sativum L.	Garden cress
Lilium longiflorum	Long-flowered white lily
Lilium superbum L.	Turk's cap lily
Linum usitatissimum L.	Common flax
Liquidambar styraciflua L.	Sweet gum
Lobelia inflata L.	Lobelia
Narcissus pseudo-narcissus L.	Daffodil
Nerium oleander L.	Oleander
Oenothera biennis L.	Evening primrose
Oxdendrum arboreum DC.	Sorrell-tree
Pastinaca sativa L.	Parsnip
Phacelia infundibuliformia Torr.	
Phleum pratense L.	Timothy
Phytolacca decandra L.	Pokewood
Picea canadensis (Mill) BSP.	White spruce
Podophyllum peltatum L.	May-apple
Polygonum acre HBK.	Water smartweed
Polygonum hydropiper L.	Smartweed
Polygonum punctata Ell.	Dolled smartweed
Populus candicans Ait.	Balm of Gilead
Primula farinosa L.	Bird's-eye primula
Psoralea esculenta Pursh.	Pomme de prairie
Puccinia graminus Pers.	
Ranunculus californicus.	
Ranunculus sceleratus L.	Cursed crowfoot
Rhus toxicodendron L.	Poison ivy
Rhus vernix L.	Poison sumac
Roripa armoracia (L) Hitchcock.	Horseradish
Ruta graveolens L.	Garden rue
Sanguinaria canadensis L.	Blood root
Sassafras varifolium (Salisb.) Katzl.	Sassafras
Sedum acre L.	Mossy stonecrop
Sicyos angulatus L.	Bur cucumber
Sisymbrium officinale (L) Scop.	Hedge mustard
Stillingia sylvatica L.	Queen's delight
Symplocarpus foetidus (L) Nutt.	Skunk cabbage
Syringa vulgaris L.	Lilac
Thuja occidentalis L.	Arbor vitae

Scientific Name	Common Name
Toxylon pomiferum Raf	Osage orange
Tropoleum majus L.	Nasturtium
Urtica chamaedryoides Pursh.	Nettle
Urtica dicia L.	Stinging nettle
Urtica gracilis Lit.	Slender nettle
Urtica urens L.	Small nettle
Veratrum viride L.	American hellebore
Verbascum thansus L.	Common mullein

TROPICAL PLANTS PRODUCING DERMATITIS [4]

Genus	Species	Common Name
Anacardiaceae	Comocladia dentata, Jacquin	Guao
	Comocladia glabra, Sprengel, variety acuminata	Guao
	Comocladia hollokii, Britton	Guao
	Comocladia grandidentata, Britton	Guao
	Comocladia Ehrenbergii, Engler	Guao
	Comocladia parvifolia, Britton	Guao
	Comocladia cordata, Britton	Guao
	Comocladia pubescens, Engler	Guao
	Comocladia jamaicencis, Britton	Guao
	Comocladia velutina, Britton	Guao
	Comocladia pilosa, Britton	Guao
	Comocladia ondulata, Urban	Guao
	Comocladia intermedia, Wright	Guao
	Comocladia platyphilla, Richard	Guao
	Comocladia dominguensis, Britton	Guao
	Comocladia dodonaeae, Britton	Guao
	Comocladia acuminata, Britton	Guao
	Metropium browneii, Urban, or M. toxiferum, Linné	Guao de costa
	Anacardium occidentale, Linné	Marañón
	Rhus venosa, Grisebach	
	Rhus metropium, Linné	
Leguminosae	Mucuna pruriens, DeCandolle, or Dolichos pruriens, Linné, or Stizolobium pruriens, Medicus	Pica-pica, cowhage, cowitch
Euphorbiceae	Platygyne pruriens, Baillon or Platygyne urens, Linné	Pringamoza
	Tragia volubilis, Linné	Pringamoza morada
	Jatropha urens, Linné	Chaya
	Hura crepitans, Linné	Salvadera
	Euphorbia lactea, Haworth	Cardon
	Jatropha curcas, Linné	Piñón de botija
	Hippomane mancinella, Linné	Manzanillo
	Acidoton urens, Sw.E	
	Acidoton microphyllus, Urban	

4. Pardo-Castello, V.: Dermatitis Venenata, Arch. Dermat. & Syph. **7**:81 (Jan.) 1923.

Genus	Species	Common Name
Urticaeae	Fleurya umbellata, Weddell	Ortiguilla
	Fleurya aestuans, Guadichard-Beupré.	
	Urera baccifera, Guadichard-Beupré.	Chichicate
	Urera dominguensis, Urban	
Malpighiaceae	Malpighia urens, Linné	
Malvaceae	Malchra urens, Poiteau	Malva Santo Domingo
Lytrareae	Cuphea urens, Kaehne	
Araceae	Phylodendrum consanguineum, Schott.	
Apocinaceae	Tabernaemontana citrifolia, Linné	Pegojo

UNCLASSIFIED CUTANEOUS IRRITANTS IN ALPHABETICAL ORDER

Acetate of iron
Acetic acid [5] (hat-makers', cleaning bottles, cleaning bronze objects)
Aceto-arsenite of copper
Acid bichromate
Acid chrome
Acid calcium phosphate
Acridine
Actinic rays (sun, electric arc)
Adhesive [6] (turpentine and resin)
Alcohol (denatured)
Amber (bakelite)
Amber liquid (stryaciflua)
Amidophenyl mercaptan vapors
Ammonia (gluteal region [7])
Ammonium chloride
Ammonium nitrate
Amyl acetate
Amyl acetone
Anthracene
Antimony pentasulphide
Aristol
Arnica
Arsenic (preservative for corpses and hair for hats)
Arsenic white (stuffing animals and destruction of vermin)
Arsenic trichloride
Arsenite of lead
Arsenous acid
Arsenous oxide
Artificial silk
Asparagus [8]
Asphalt
Atropine
Aurantia (cheap shoe dye)
Bakelite (amber [9])
Baker's dermatitis [10] (salt, sugar, cream, powder, acid phosphate of lime)
Barley pollen [11]
Beet-sugar
Benzine
Betel-nut chew [12]
Bichromate of mercury
Bichromate of potassium

5. Carozzi, L.: Acetic Acid, Occupation and Health Brochure 33, Geneva, International Labour Office.

6. Brown, W. P.: Sensitization to Adhesive Plaster, Arch. Dermat. & Syph. **12**:69 (July) 1925.

7. Cooke, J. V.: Etiology and Treatment of Ammonia Dermatitis of Gluteal Region of Infants, Am. J. Dis. Child. **22**:481 (Nov.) 1921; abstr., J. A. M. A. **77**:1762 (Nov. 26) 1921.

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10. Parsons, Allan C.: Bakers' Dermatitis, Brit. J. Dermat. **36**:193, 1924.

11. Hodera, M.; Behjet, H., and Sureya: Barley Pollen, Dermat. Wchnschr. **76**:209 (March 10) 1923.

12. Mendelson, R. W.: Tinea Labialis (Betel-Nut Dermatitis of Lips), J. Trop. Med. **27**:284 (Nov.) 1924.

Unclassified Cutaneous Irritants in Alphabetical Order—*Continued*

Bichromate salts (dust)
Bichromate of soda
Biniodide of mercury (sodium iodide and ammoniated mercury)
Bismarck brown
Bitter oranges [13]
Black cotton shirts
Blue print [14] (bichromate of potassium)
Bookbinders (glue and formalin)
Boric acid and borax [15]
Briquette making
Bromine trifluoride
Brown tail moth
Butesin picrate [16]
Butyn [17]
Calcium hydrate
Calcium hypochlorite
Cantharides
Carbide
Carbon disulphide
Carpoglyphus passularum [18] (figs covered with)
Caustic potash
Caustic soda
Celery juice [19]
Cement
Chocolate dippers [20]
Chrome colors
Chrome orange
Chrome yellow
Chromyl chloride vapor
Chrysarobin
Cinchona bark
Citronella (Weber)
Cocoa butter
Colored paper (school-girl [21])
Common parsnip [22]
Copper itch [23]
Copra [24]
Cotton seed [25]
Cotton shirts
Croton oil
Cyanide solution [26]
Depilatories (barium and calcium sulphide)
Dermax (Turkey red oil)
Dichloramin-T

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13. Murray, F. A.: Dermatitis Caused by Bitter Oranges, Brit. M. J. **1**:729 (May 21) 1921.

14. Parkhurst, H. J.: Dermatosis Industrialis in a "Blue Print" Worker Due to Chromium Compounds, Arch. Dermat. & Syph. **12**:253 (Aug.) 1925.

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17. Greenwood, Arthur M.: Butyn Dermatitis, J. A. M. A. **83**:1077 (Oct. 4) 1927.

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21. Rowell, Hugh Grant: An Unusual Case of Dermatitis Venenata Caused by Colored Paper, Arch. Dermat. & Syph. **7**:603 (May) 1923.

22. White: Common Parsnip, J. Cutan. Dis. **14**:441, 1896.

23. "Copper Itch," Query and Minor Note, J. A. M. A. **86**:971 (March 27) 1926.

24. Castellani, Aldo: Note on Copra Itch, J. Trop. Med. **15**:274, 1912.

25. Nixon, J. A.: Cotton Seed Dermatitis, Brit. J. Dermat. **27**:122, 1915.

26. Burke, J. G.: Occupational Dermatitis from Cyanide Solution, Arch. Dermat. & Syph. **5**:282 (Feb.) 1922.

Unclassified Cutaneous Irritants in Alphabetical Order—*Continued*

Dinitrochlorbenzine
Dust
Dyanshine (Bismarck brown) (Pusey and Weber)
Emerald green
Ephedrine dermatitis [27]
Ethyl acetate (Weber)
Ethylene chloride
Feathers [28]
Felt hat
Fertilizers
Figs
Flax and flax dust [29]
Flit (insect) [30]
Flour
Formaldehyde
Formic acid
Fruits
Fuchsin
Fur dyes
Furniture polish
Gasoline
Geranium [31]
Golden rod pollen
Grain
Guinea-pig hair
Hair dyes
Hat bands (artificial) [32]
Hay and straw
Hemp
Hop (plant) [33]
Hop hornbeam [34]
Horn rim spectacles [35]
Humea elegans
Hydrocyanic acid
Hydrofluoric acid
Hypochlorites
Inecto hair dyes
Ink, printers' [36]
Insect powder [37]
Iodine and its compounds
Iodoform
Jute [38]
Kabiline (dye for a waist) [39]
Kerosene
Lacquer [40]

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27. Scheer, Max: A Case of Dermatitis Venenata Due to Ephedrine, Arch. Dermat. & Syph. **20**:641 (Nov.) 1929.

28. Abramowitz: Dermatitis Due to Feathers (?), Arch. Dermat. & Syph. **16**:773 (Dec.) 1927.

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32. Galewsky, E.: Dermatitis After Substitutes, Klin. Wchnschr. **3**:1767 (Sept. 23) 1924.

33. O'Donovan, W. J.: Hop Dermatitis, Lancet **2**:591 (Sept. 20) 1924.

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35. Sutton, J. C.: Acute Dermatitis from the Wearing of "Horn-Rim" Spectacles, J. A. M. A. **89**:1059 (Sept. 24) 1927.

36. Industrial Dermatoses Among Printers, Miscellany, J. A. M. A. **77**:1760 (Nov. 26) 1921.

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38. Curjel, D. F., and Acton, W. H.: Jute Dermatitis, Indian J. M. Research **12**:257 (Oct.) 1924.

39. Hudelo and Dumet: Dermatitis from a Waist Dyed with "Kabiline," Bull. Soc. franç. de dermat. et syph. **29**:92, 1922.

40. Pusey, William Allen: Lacquer Dermatitis, Arch. Dermat. & Syph. **7**:91 (Jan.) 1923.

Unclassified Cutaneous Irritants in Alphabetical Order—*Continued*

Lampblack [41]
Lead arsenate
Lead salts
Lime [42]
Linseed oil [43]
Lyddite
Lye (washerwomen's dermatitis)
Lysol
Macassar oil
Mah Jongg sets
Margarine
Marigold (Legion of Honor)
Match-box (phosphorus) [44]
Melinite
Mercury and compounds
Mercuric chloride
Mercuric bichromate
Mercury fulminate
Metol and hydroquinone developer [45]
Mica (aluminum silicate)
Mohair [46]
Morphia
Mouth washes (01. menth. pip. 01. Caryophyll, formaldehyde, salol, Tr. arnica)
Mustard gas
Naphtha
Nerium oleander
Oak [47]
Oilcloth [48]
Oil of cassia
Oleic acid [49]
Oriental cashew
Orris root powder [50]
Orthoform [51]
Oxalic acid
Paint solvents (turpentine and naphtha) [52]
Paraphenylendiamine
Patent cleaners
Patent soap powders
Peas
Perfume
Peruvian balsam [53]
Petroleum
Phenol and its derivatives
Phosphorus (match-box)
Photodermatitis (sunlight)
Picric acid [54]
Pictorial papers (rotogravure) [55]

41. Dermatitis Due to Lampblack, Query and Minor Note, J. A. M. A. **68**:799 (March 10) 1917.

42. O'Donovan, W. J.: Lime Dermatitis, Lancet **1**:599 (March 21) 1925.

43. Vokoun, F. J.: Linseed Oil Dermatitis, J. A. M. A. **89**:20 (July 2) 1927.

44. Frei, W.: Match-Box Dermatitis, Med. Klin. **17**:461, 1921.

45. Beevo, Nathan T.: Metol Dermatitis, New York M. J. **88**:506 (Sept. 12) 1908.

46. Rowe, A. H., and Rogers, H.: Allergic Dermatitis: Case Due to Mohair, California & West. Med. **23**:1589, 1925; abstr., J. A. M. A. **86**:306 (Jan. 23) 1926.

47. Spillmann, L.: Artificial Dermatitis Due to the Action of Oak (Quercus rober), Bull. Soc. franç. de dermat. et syph. **6**:33, 1921.

48. Dreyer: Oilcloth Dermatitis, München. med. Wchnschr. **68**:1000, 1921.

49. Hailey, W. H.: Dermatitis from Oleic Acid, Arch. Dermat. & Syph. **8**:530 (Oct.) 1923.

50. Marlow, F. W.: Itching of Eyelid Due to Allergic Reactions, Am. J. Ophth. **10**:52 (Jan.) 1927.

51. Shelmire, J. B.: Report of Cases, Texas State J. Med. **11**:1, 1915; abstr., J. A. M. A. **64**:2021 (June 12) 1915.

52. Turner: Paint Solvents Cause a Dermatitis, J. Indust. Hyg. **7**:293 and 344 (July) 1925.

53. Cummer, C. L.: Dermatitis Produced by Balsam of Peru, Arch. Dermat. & Syph. **16**:44 (July) 1927.

54. Bernard-Ballet: Two Cases of Generalized Dermatitis Following Moist Applications of Picric Acid, Bull. Soc. franç. de dermat. et syph. **30**:34, 1923.

55. Oliver, E. A.: Rotogravure Ink Dermatitis, J. A. M. A. **91**:870 (Sept. 23) 1928.

Unclassified Cutaneous Irritants in Alphabetical Order—*Continued*

Plaster
Portuguese Man-of-War [56]
Procaine
Pyrethrum
Pyrogallic acid
Ragweed [57]
Rattan
Reeds
Resin [58]
Resorcin [59]
Rice [60]
Rubber industry (hexanitrodiphenylamine)
Rulers (Maracaibo and African Boxwood)
Sand
Sealing wax [61]
Silk
Silk (artificial)
Soaps
Soap powders
Sodium arsenate
Sodium chloride
Sodium hydroxide
Sodium salicylate
Sorghum cutters (parasite)
Stearic acid
Stockings (erythrosin, eosin, aurin)
Sugar
Tallow
Tanners (lime, arsenic sulphide, chrome acid)
Tannin
Tear gas (Chloracetephenol) [62]
Tetrachlorethane
Tetranitromethylaniline
Tetryl
Thorium
Tin foil
T. N. T.
Tobacco leaf
Trinitroluen
Tulip bulbs [63]
Turkey red
Turpentine
Urotropine
Vanilla
Varnish
Wall paper cleaner
Wartaric acid
Water glass (silicate of sodium)
Witch-hazel
Wood alcohol
Wood turpentine [64]
Yellow ochre

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56. Crutchfield, E. D.: Dermatitis Produced by the Portuguese Man-of-War, Arch. Dermat. & Syph. **12**:72 (July) 1925.

57. Hannah, Louis: Ragweed Dermatitis, J. A. M. A. **72**:853 (March 22) 1919.

58. Beinhauer, L. G.: Resin Dermatitis: Report of Case, J. A. M. A. **81**:13 (July 7) 1923.

59. Taylor: Dermatitis from Resorcin, J. Cutan. Dis. **12**:169, 1895.

60. Anderson and Rawlins: Rice Dermatitis, California & West. Med. **23**: 42 (Jan.) 1925.

61. Kleeberg: Dermatitis Due to Sealing Wax, Arch. f. Dermat. u. Syph. **138**:360, 1922.

62. Crawford: Tear Gas Dermatitis, Arch. Dermat. & Syph. **14**:95 (July) 1926.

63. Overton, Sibyl G.: Tulip Bulb Dermatitis from Handling, Lancet **2**:1003 (Nov. 13) 1926.

64. McCloud, C. P.: Occupational Dermatitis from Wood Turpentine, J. A. M. A. **86**:1979 (June 26) 1926.

HEPATORECURRENT SYPHILIS

REPORT OF A CASE TERMINATING IN ACUTE YELLOW ATROPHY *

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It is generally admitted that one of the most vexing problems in syphilology today is the pathogenesis of, and more particularly the best therapeutic procedure in, icterus developing during or after a course of organic arsenical injections. In this regard, the most recent opinions of Milian, Ravaut and a number of other French authors are of special interest. On the basis of a study of 118 cases of icterus of this sort, Milian [1] insisted on the continued use of the arsenical compounds in post-therapeutic types of icterus or in those developing from two weeks to several months or more after the last injection. He believed all of these to be of a syphilitic nature, and he stands almost alone in his therapeutic advice. Of 105 patients who had received treatment before the icterus developed, 75 had this post-therapeutic type.

Ravaut,[2] Lortat, Jacob, Sezary and Simon,[3] with 111 cases among them, advised the cessation of all arsenical compounds once icterus has developed, whether it develops during or after a course of treatment and irrespective of its syphilitic nature. If one suspects the icterus to be syphilitic, it is preferable to resort to other antisyphilitic drugs such as mercury and bismuth. The report of this case is prompted not so much because of its rarity, but more especially because of the therapeutic problem involved and because I believe it appears to clarify the therapeutic situation in at least one type of icterus occurring during the course of syphilis, namely, that developing in syphilitic patients sometime after they have received a partial course of injections of one of the arsphenamines.

REPORT OF A CASE

History.—K. P., a negress, aged 22, single, came to the clinic of Dr. J. Frank Schamberg on July 2, 1929, complaining of pain in the vagina of several weeks' duration. The only thing of special interest in the previous history was that she had suddenly developed a generalized eruption on Dec. 28, 1928, together with general malaise, headache and sore throat. She consulted a physician who had a Wassermann test of the blood made which showed a reaction of 2 plus. The subsequent history was verified by the social service department and later by myself.

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* Submitted for publication, Oct. 24, 1929.

* From the Graduate School of Medicine of the University of Pennsylvania.

1. Milian, G.: Bull. Soc. franç. de dermat. et syph. **9**:873, 1928.
2. Ravaut, P.: Bull. Soc. franç. de dermat. et syph. **8**:818, 1928.
3. Lortat; Jacob; Sezary and Simon: Bull. Soc. franç. de dermat. et syph. **9**:865, 883, 891, 1928.

On Feb. 22, 1929, the physician gave the patient neoarsphenamine (Metz) 0.3 Gm. intravenously; on March 1, 8 and 15, 0.45 Gm., respectively. As no reactions resulted, the patient did not return for further treatment. In fact, she said that she had not received any further treatment until the time she presented herself at the clinic, three and one-half months later.

Physical Examination.—The patient was well nourished and did not appear ill. The essential features of the case were: (1) intensely jaundiced conjunctivae; (2) pinhead and slightly larger-sized, rounded, pigmented remains of a generalized exanthem such as is usually seen in the colored race following the small papulopustular syphiloderm; (3) a dollar-sized, tender, irregular ulceration of the posterior vaginal wall suggestive of an ulcerated secondary lesion, and not so painful as chancroid; (4) impalpability of the liver, which appeared smaller on percussion.

On the basis of the history and the physical examination, the diagnosis of a hepatorecurrence appeared certain, and she was given 100 mg. of potassium bismuth tartrate intramuscularly. It was intended to repeat the treatment twice weekly. The thought of a condition so rare as icterus gravis and under such circumstances never entered my mind. I might add that although I would have liked to have continued the treatment with neoarsphenamine, I was deterred by the literature on the subject and by an unfortunate previous experience quoted later.

Three days later, the patient was brought into the hospital in a semiconscious state. She had become more or less stuporous twenty-four hours previously, that is, on July 4, two days after visiting the clinic. She was incontinent and in a mild muttering delirium. The temperature and respiration were normal, but the pulse rate was 120; all three reactions, however, increased twenty-four hours before death.

Laboratory Studies.—A van den Bergh test given on the day of admission gave a strong immediate reaction (22.5 mg. bilirubin per hundred cubic centimeters). The blood urea was normal, but dextrose was reported as 50; it mounted to 420 the next day. The blood picture showed red cells, 3,140,000; white cells, 9,800; hemoglobin, 60; polymorphonuclears, 90. No examination was made for leucine or tyrosine, and it was impossible to make an examination of the urine.

Course.—A generalized discrete petechial eruption developed the day before death. I saw the patient late on July 5, when a tentative diagnosis of acute yellow atrophy of the liver was made which was later confirmed at autopsy. Despite intravenous injections of sodium thiosulphate, dextrose and sodium iodide, she gradually lapsed into a coma and died July 6, thirty-six hours after admission.

Postmortem Report (Dr. Eugene Case).—The patient, a young, well developed, muscular negress, died on July 6, 1929, at 3:20 p. m. Autopsy was performed July 7 at 10 a. m.

On the face, torso and lower limbs were the pigmented remains of a rash, and the conjunctivae showed intense jaundice. The peritoneal sac contained from 100 to 200 cc. of bloody fluid, the blood oozing from the large areas of hemorrhagic extravasation in the omentum, mesentery, parietal peritoneum and the retroperitoneal fat. She had had an extensive pelvic inflammation which had caused adhesions too tough to separate without dissection to develop, and which had involved all of the pelvic viscera. The obliteration of both pleural sacs by fibrous adhesions explained a former pleuritis.

The chief interest in the autopsy centered about the liver, though changes were present in other organs. The liver was a pale brownish color and small, weigh-

ing only 510 Gm., a marked disproportion in weight as compared with the size and development of the patient. The capsule appeared to be slightly thickened, probably the result of a shrinkage of the capsule in accommodating itself to the reduced size of the organ. The edges were sharp, and along them the liver was thin and atrophic. The organ was flabby, the tissue was somewhat friable, and the cut surface showed irregular light yellow areas which formed a contrast to the brownish red of the rest of the tissue.

The gallbladder was not inflamed and contained only a small amount of thick greenish bile.

The kidneys were pale, the vessels were congested, and the capsules were stripped easily. They were soft, and the cut surface was dull and lusterless. The congested vessels appeared as reddish streaks and dots. The picture was that of an acute nephrosis plus postmortem degeneration.

Histologic Study.—Postmortem changes were extensive, masking the alterations of the disease.

Undoubtedly, the pathologic products present at death had accelerated autolysis. However, in the liver it was evident that disease had played a large part. This organ was hardly recognizable, as its normal architecture was much disturbed. No normal liver cells were to be seen, many having completely disappeared. Others were ragged, granular, anuclear masses of protoplasm, while a few still retained poorly stained nuclei surrounded by shrunken, ragged cytoplasm. Even the bile ducts showed cell destruction and were not easily recognized.

Between the lobules, which were comparatively few and widely separated, there was considerable cellular infiltration of lymphocytes and mononuclear wandering cells, some of which were phagocytic and contained ingested débris and degenerated cells. This infiltration was densest in the interlobular zones, but the cells had also wandered into the lobules.

The extent of the destruction and tissue loss can be realized when one remembers that almost two thirds of the normal weight of the organ had disappeared.

In the kidney, postmortem autolysis played such a large part that the real pathologic change was obscured.

The other organs showed no noteworthy change.

Pathologic Diagnosis.—The anatomic diagnosis was: secondary syphilitic eruption; jaundice; ascites with blood-stained fluid; chronic fibrous pelvic adhesions; hemorrhagic extravasations in the omentum, mesentery and retroperitoneal tissue; blood-stained fluid in the pericardium; slightly dilated heart; myocardial degeneration; chronic, obliterative, fibrous adhesions of both pleurae; edema and congestion of and hemorrhage into the lungs; slightly enlarged spleen; acute toxic nephrosis; healed chronic oophoritis and salpingitis; distention of the stomach with the presence of bloody fluid, and toxic hepatitis of the nature of acute yellow atrophy.

The histologic diagnosis was: extensive postmortem autolysis of all the organs, acute toxic nephrosis (?) and acute yellow atrophy of the liver.

COMMENT

Following the autopsy, the question naturally arose in the minds of those who saw the patient as to whether the entire picture could not be that of a purely arsenotoxic rather than of a syphilotoxic condition. Although not conclusive, there were, however, a number of reasons against believing it an arsenical condition.

First, the universal phobia, with which the arsphenamines are regarded in relation to toxicity of the liver, is largely based on the known intolerance of the liver to inorganic arsenic, but it is rarely recalled that this is a result of prolonged oral dosage, the tendency of the liver to store arsenic and an accumulative effect. Even if such were true of the arsphenamines, it would then have to be assumed that they could be used as substitutes in the diseases in which inorganic arsenic is almost specific. However, clinical experience indicates that this is not so, since in those instances in which inorganic arsenic by mouth or by injection is of value, poor or no results are obtained with the arsphenamines. In such a connection, the toxicologic studies of the neoarsphenamines by Kolmer and Lucke [4] cannot be entirely ignored despite the fact their experiments were conducted with fifteen times the therapeutic dose in man. In a given case in which there is intolerance to even a therapeutic dose of neoarsphenamine, the histologic changes caused in the liver by the intoxication will undoubtedly approximate those found in the experimental animal by the authors mentioned.

Second, hepatic function tests [5] of patients who have received and have apparently tolerated as high as 124 intravenous injections of one or both arsphenamines have failed to show any interference in the liver's excretory power for tetrachlorphthalein. In the third place, although it is true that the arsphenamines in therapeutic dosage may be and have been toxic for the liver in intolerant patients, under such conditions the hepatic disturbances are commonly accompanied by signs of intoxication involving other structures, and they generally develop within from one to two weeks after the use of the drug. Lastly, there is no known drug that, in tolerated doses, as it was in this patient, in such small amounts will produce poisoning almost four months after its ingestion.

From the foregoing facts, one should be able to exclude definitely toxic hepatitis. Had the patient received a further injection the day she was admitted to the clinic, many would, doubtless, have interpreted the autopsy observation as showing a clearcut toxic arsenical condition.

When the patient was first seen, a diagnosis of catarrhal jaundice was also considered, but the absence of fever, gastro-intestinal disturbances, coated tongue, the history and the remains of the secondary lesions, practically excluded it. I am not certain that a nonsyphilitic infectious condition such as catarrhal icterus would be made worse by the administration of the arsphenamines. In fact, they are often used for a variety of infections, such as pyelitis and puerperal sepsis.

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4. Kolmer, J. A., and Lucke, R.: Study of Histologic Changes by Neoarsphenamin, Arch. Demat. & Syph. **3**:514 (April) 1921.

5. Greenbaum and Brown: Tetrachlor Liver Test in Cases of Acute and Chronic Syphilis Under Treatment, J. A. M. A. **82**:88 (Jan. 12) 1924.

The question, therefore, is: Could one assume that the condition was recurrent syphilitic hepatitis?

SYPHILITIC RECURRENCES

Many thousands of patients with syphilis have received but three or four treatments with one of the organic arsenical drugs, only to stop treatment and permit weeks and months to elapse until syphilitic recurrences compelled them again to seek aid. Under such insufficient therapeutic conditions, irrespective of the drug, more commonly after the arsenical injections, syphilitic recurrences, particularly in the blood, skin and the central nervous system, are far from uncommon. Serologic relapses in particular are extremely common even after fairly satisfactory treatment. Such neurologic, serologic and cutaneous recurrences are well recognized entities the therapeusis of which is clear. It is likewise known that they are most apt to follow secondary syphilis for which the patient has been insufficiently treated. Although the recurrences are common in the blood, skin and central nervous system, they are rare in the liver, at least in a gross enough manner to produce symptoms and signs. They occur, of course, but it is exceedingly rare to see them in the form of acute yellow atrophy as occurred in this patient.

It must be admitted in a good many instances that the time when the icterus appears as related to the last injection is not always helpful from the standpoint of pathogenesis, particularly if the icterus developed during or shortly after the treatment. This was well illustrated in the case reported by Schamberg and myself,[6] in which a patient with secondary syphilis (relapsing iritis) developed icterus after four injections of neoarsphenamine given over a period of one month, and it was assumed that we were dealing with a herxheimer reaction. Resumption of treatment was followed by polyneuritis. It should be added that Milian differs in the interpretation of the pathogenesis of both the jaundice and the polyneuritis in this case and in a similar one reported by Ravaut.[2]

Icterus gravis syphiliticus, of which the case reported here appears to be an example, is a rare but well recognized disease.[7] In most of the reported cases, it developed in untreated patients with secondary syphilis, thus clearly indicating its syphilitic nature. That it may develop as a fulminating hepatorecurrence is not generally known, due, in a large measure, to the paucity of postmortem reports of cases such as the one here described.

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6. Schamberg and Greenbaum: Multiple Neuritis with Jaundice After the Use of Neoarsphenamine, J. A. M. A. **84**:163 (Jan. 17) 1925.

7. Stokes, J. H.: Modern Clinical Syphilology, Philadelphia, W. B. Saunders Company, 1927, p. 770.

In view of the fact that any icterus developing one or more months after a course of arsphenamine therapy may represent a fulminating relapse of this sort, I am persuaded to believe that Milian is correct in at least part of his therapeutic stand. Since I already had evidence that this patient had been tolerant to arsphenamine and for the aforementioned reasons concerning arsenotoxicity, it seemed that no harm could have resulted from the further use of the drug in this particular instance, even if the icterus gravis was not syphilitic.

While it is true that it is best to avoid arsenic in icterus developing during the course of treatment, certainly it seems as if the pendulum has swung too far and that at least the post-therapeutic types of icterus should not be included in their entirety in this category.

SUMMARY AND CONCLUSIONS

1. An instance is reported of hepatorecurrence terminating in acute yellow atrophy in a patient, who three and one-half months previously received four small intravenous injections of neoarsphenamine for secondary syphilis.

2. Intravenous injections of sodium thiosulphate, dextrose and sodium iodide and a single intramuscular injection of bismuth, did not stay the progress of the disease.

3. The use of the slow-acting drugs, bismuth and mercury, appears inadvisable in clearcut instances of hepatorecurrence.

4. Arsenical therapy in maximum tolerated doses is not always contraindicated in patients with syphilis who develop icterus one or more months after the last treatment. This is especially true of those whose course of treatment had been insufficient.

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SUBCUTANEOUS CYSTICERCOSIS CELLULOSAE IN MAN

A REPORT OF FIVE CASES *

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The localization of *Cysticercus cellulosae* in the subcutaneous tissues of man was reported by Lewin [1] as having occurred in some of the early cases of cysticercosis first recognized in Europe in the middle of the sixteenth century. Pye-Smith,[2] in 1892, reported a case from England in which there were more than fifty tumors scattered over the face, neck, trunk and extremities, the exact nature of which was demonstrated by microscopic examination of the encysted organism. More recently, Waterhouse [3] and Priest [4] in England and Coblentz [5] in America published reports of cases of the subcutaneous type, and Africa and Cruz [6] in the Philippine Islands described the localization of the cysts in the skeletal muscles of man. At times, subcutaneous and visceral involvement are present in the same patient. Of all forms of *Cysticercus* infestation, only three cases have been reported in China.[7]

That this condition is not as rare in China as the records indicate is suggested by the present report which deals with six cases diagnosed in the Peiping Union Medical College Hospital during a period of ten years. Five of these were observed during the past two years.

LIFE CYCLE OF TAENIA SOLIUM

The natural intermediate host of the pork tapeworm, *Taenia solium*, is the pig, in the muscles of which *Cysticercus cellulosae* develops from

* Submitted for publication, Jan. 17, 1930.

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1. Lewin, G.: Arch. f. Dermat. u. Syph. **26**:71 and 217, 1894.
2. Pye-Smith: Brit. J. Dermat. **4**:366, 1892.
3. Waterhouse, R.: Quart. J. Med. **6**:469, 1912-1913.
4. Priest, R.: Brit. M. J. **2**:470, 1926.
5. Coblentz, Z. B.: Cysticercus of Skin, J. A. M. A. **85**:1136 (Oct. 10) 1925.
6. Africa, C. M., and Cruz, J. Z. S.: J. Philippine Islands M. A. **7**:209, 1927.
7. Mills, R. G.: China M. J. **38**:465, 1924.

an onchosphere set free by the action of gastric juice on the shell of the ovum of the adult worm. The onchospheres work their way through the gastric mucosa into the blood stream and are carried to the muscles, where they become encysted. The infection is transmitted to man through the eating of infected or so-called "measly" pork, which contains the cysticercal worm. After digestion of the wall of the cyst and after extrusion of the larva, the scolex anchors by means of its hooks to the mucosa of the small intestine, where it grows into an adult tapeworm. The free ova or proglottides are discharged with the feces and and are later ingested by the pig, completing the normal life cycle of the organism.

Under certain circumstances, man acts as the intermediate host instead of the pig. Either by the eating of contaminated food or by regurgitation during the act of vomiting, ova or ripe proglottides are introduced into the stomach and there develop into onchospheres. These gain entrance into the general circulation through the gastric mucosa and are disseminated to various organs or tissues of the human body, where they encyst and produce such symptoms as may be characteristic of a tumor localized in the organ or tissue of their encystment. The cysticercus slowly degenerates and may become calcified. Osler [8] reported a case in which hundreds of subcutaneous nodules proved to be calcified cysticerci.

Of the present series of six patients, five had involvement of the subcutaneous and muscular tissues, and one had a lesion located in the cerebral cortex. Vosgien [9] collected 807 reports of cases of somatic teniasis, chiefly from Europe. In about 6 per cent of these cases, the subcutaneous connective tissue was the site of the cysticercus; in about 3 per cent, the muscles; and in 86 per cent, the eyes and adnexa and the central nervous system were involved in about equal proportions. Almost any organ or tissue may be invaded, the heart, lung, pancreas and peritoneum included.[10]

An unusual feature of two of the present cases was the fact that the patients served as both definitive and intermediate hosts, for the tapeworm was harbored in their intestines and the cysticercus in their somatic tissues. A knowledge of the frequency of this occurrence cannot be gained from the literature, as many writers fail to report the results of fecal examinations. Lewin cited a number of instances in which the patients also had *Taenia solium* in the intestines. Of the fourteen patients with cysticercosis whom he had personally seen, three

8. Osler, William, quoted by Roth, E. J. H.: Brit. M. J. **2**:471, 1926.

9. Vosgien, Y.: Le cysticercus cellulosae chez l'homme et les animaux, Paris, 1911; quoted by Africa and Cruz (footnote 6).

10. Lewin (footnote 1). Abbott, H. K.: Lancet **2**:956, 1921.

harbored the intestinal tapeworm. One case of this nature, in which the eye was the site of encystment, was reported by de Schweinitz and Wiener.[11]

REPORT OF CASES

CASE 1.—A Chinese man, aged 28, came to the outpatient department of the Peiping Union Medical College Hospital on Dec. 19, 1928, complaining of multiple painless nodules underneath the skin. The first nodule was noticed over the right

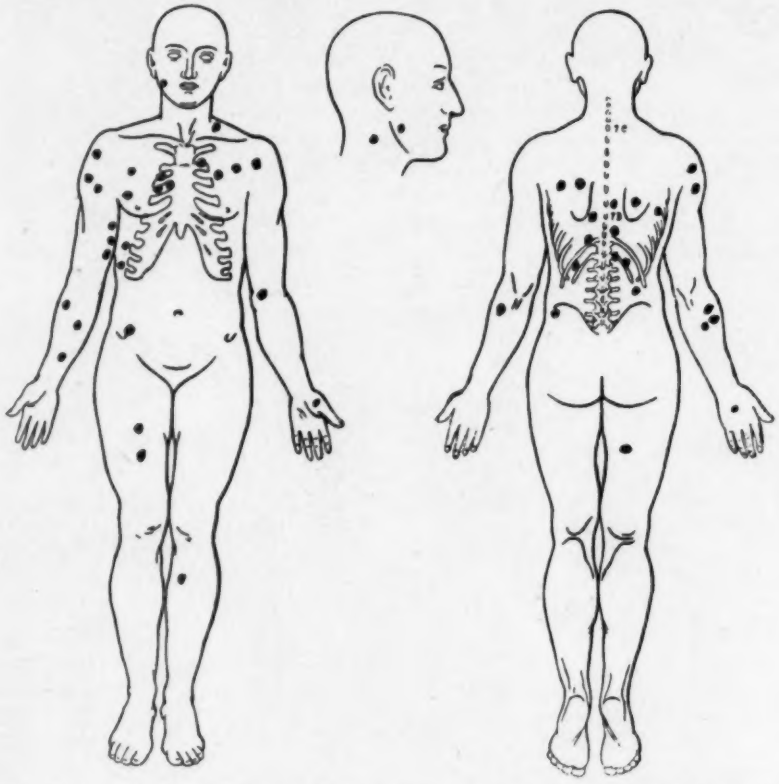

Fig. 1 (case 1).—Distribution of subcutaneous tumors (*cysticercus cellulosae*).

flank thirteen months before. Following that, a few new ones appeared every month. Each nodule was at first the size of a millet seed and gradually grew to about 1.5 cm. in diameter. These nodules had never been painful or tender, but sometimes they "felt numb" and occasionally were "itchy." They had never moved from place to place. The only constitutional symptoms were an occasional sensation of chilliness and muscular weakness during the preceding year.

The patient was a farmer and had close contact with horses and cattle, but not with swine. Even on close questioning, he denied having eaten any uncooked

11. De Schweinitz, G. E., and Wiener, M.: 1. Cysticercus of the Vitreous. 2. Congenital Multinocular Cysts in Relation with the Retina. 3. Anterior Lenticonus, J. A. M. A. **73**:1187 (Oct. 18) 1919.

or insufficiently cooked pork, but ten days after discharge from the hospital he returned to inform us that in October, 1926, he ate some boiled pork which contained, as he just recalled, some "bean-sized yellowish-gray waterbags." It is possible that this dated his infection. In August, 1928, he passed a white, flat, segmented worm about 1 foot (30.48 cm.) in length.

On physical examination, the organs of the head, including the eyes, and the thoracic and the abdominal viscerae were found to be normal. The muscles of the arms and legs looked normal in size, but felt flabby; the muscular power was, however, good. There were about fifty barely visible ovoid nodules underneath the skin, distributed from the face to the hands and ankles (fig. 1). The overlying skin was normal. On palpation, these nodules were freely movable and seemed to be situated in the subcutaneous tissue. They were not tender; they were firm, and fairly uniform in size, most of them being about 1 cm. in length. Two or three recent lesions measured only 0.5 cm. in diameter. From the past history of passing a segmented worm and from the character of the subcutaneous tumors, a diagnosis of cysticercosis was made.

Examination of Tumors.—At operation, on dissection of the muscles, a small cyst popped out, but remained attached on one side (fig. 2). Inside the wall of the cyst was a small, yellowish, opaque mass about 0.3 cm. in diameter, floating

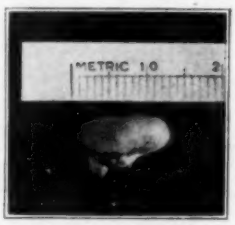

Fig. 2.—Cyst removed from subcutaneous tissue, showing pedicle by which it was attached.

in a clear fluid. Another specimen was removed for dissection and identification of the larva. The outer wall of the cyst was composed of fibrous tissue about 0.1 cm. thick, and contained about 0.3 cc. of clear serous fluid. The larva was enclosed in another thin, transparent membrane (fig. 3). When this was opened with dissecting needles under the microscope, the head protruded from the bladder portion and moved for a short time. The larva, which was identified as *Cysticercus cellulosae,* is shown in figure 4.

Skin Sensitization Test.—Some of the clear fluid of the cyst was immediately drawn into a tuberculin syringe and inoculated intradermally and by scarification into the arms of the patient. The results of the test at the end of the first twenty minutes and again on the day following inoculation were negative.

Laboratory Examinations.—The leukocyte count was 12,000, of which 75 per cent were polymorphonuclear neutrophils, 21 per cent lymphocytes, 3 per cent large monocytes and 1 per cent eosinophils. The erythrocyte count was 4,400,000, with a hemoglobin content of 85 per cent (Hellige). The Wassermann and Kahn reactions of the blood serum were negative.

The patient's stool was found to contain many ova of *Taenia.* The patient was treated with oleoresina aspidii, and on the same evening he passed a tapeworm about 7 feet in length (213.38 cm.). Segments of the worm contained uteri with from eight to twelve branches.

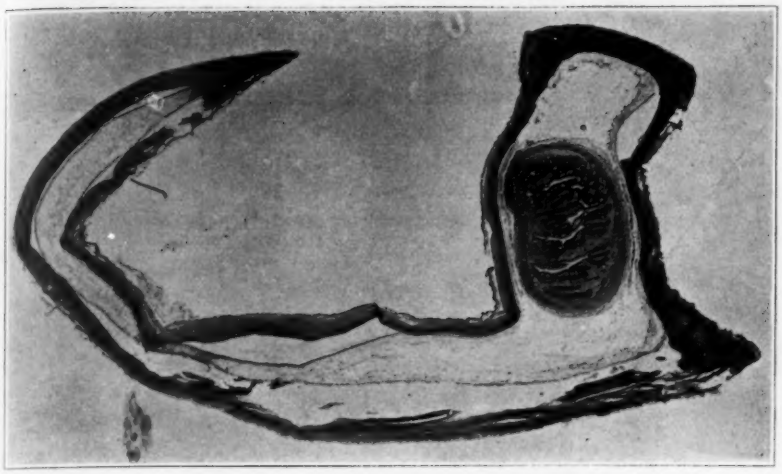

Fig. 3.—Cross-section of cyst and larva showing the thick outer fibrous wall and the thin inner membrane; × 12.

Fig 4.—The larva removed from the cyst, showing the head with four suckers and a double row of thirty-two hooklets around the rostellum, the narrow, short neck, and the distal bladder portion; × 20.

The urine contained no albumin, sugar, casts or red blood corpuscles.

Course of Disease.—The patient was examined on Jan. 16, Feb. 7 and April 4, 1929. The stools remained free from the ova of *Taenia* and no new nodules developed. All of the old lesions were still present. There was no roentgenologic evidence of calcification of the cysts.

Case 2.—This case was briefly reported by Dr. Mills.[7] A Chinese student, aged 24, who presented himself in January, 1924, had a painless tumor of the chest wall on the right. The duration of the tumor was twelve years.

On physical examination, a freely movable, firm, solitary subcutaneous nodule of the size of a bean was found. A diagnosis of fibroma was made, and excision was advised. At operation, a cyst was found lying in the pectoral muscle. A yellowish, opaque mass could be seen floating in the clear fluid inside the cyst. This was identified as *Cysticercus cellulosae.*

Laboratory Examinations.—The leukocyte count was 16,000, with 51 per cent polymorphonuclear neutrophils, 47 per cent lymphocytes, 2 per cent large monocytes and no eosinophils or basophils.

The stool was not examined.

Course of Disease.—In October, 1926, the patient returned, complaining of occipital headache, which was attributed to an acute infection of the upper part of the respiratory tract. He went to the neurologic clinic in May, 1927, again complaining of occipital headache, which was said to have been present, at varying intervals, for about three years. At this time no explanation of his headache was given. Syphilis was excluded by the negative Wassermann reaction of the blood serum. Examination of his eyes revealed only trachoma.

The patient disappeared from the clinic in June, 1927. In the thought that the headache might have been due to cysticercosis of the brain, an effort was made to bring the patient back for further examination, but he was not located.

Case 3.—A Chinese military officer, aged 23, who presented himself in January, 1927, had multiple painless nodules of one year's duration on his back, arms and abdomen (fig. 5). He had no other complaints.

On physical examination, about a dozen small, nontender, firm, freely movable subcutaneous nodules were found at the sites stated, and, in addition, one was found in the lower lip and another in the left parietal region of the scalp. The liver and spleen were enlarged. A tentative diagnosis of multiple fibromas was made.

Examination of Tumors.—One of the tumors was removed for diagnosis and was found to be a cysticercus. Four other lesions were excised. These proved to be cysticerci, and the finding of hooklets identified the organism as *Cysticercus cellulosae.*

During a period of three and a half months, the patient's stools were examined four times, and on no occasion were the ova of *Taenia* found. On account of the enlargement of the liver and the spleen, cysticerci were suspected of being present. Roentgenologic examination failed to show shadows resembling calcified cysts in the diaphragm, liver and lungs.

Case 4.—A Chinese military officer, aged 28, came to the dermatologic clinic on March 29, 1929, for treatment for multiple painless subcutaneous nodules. There were no other complaints. The first nodule appeared below the right lower eyelid a year before, and the others in the following six months. The patient was not aware that the nodules ever moved from place to place. He had never noticed any segmented worm in his stools.

On physical examination, many oval, firm, nontender, freely movable subcutaneous nodules were found over the chest, back, arms and abdomen. There were four on the face and a few on the neck and lower extremities. Altogether, they numbered about eighty. The size of the nodules varied from 0.5 to 1.5 cm. in length. The heart, lungs and abdomen were normal. The liver and spleen were not palpable. In view of the characteristic physical observations, a diagnosis of cysticercosis was made.

Examination of Tumors.—One of the tumors was removed from the chest wall on the right and was found to be a cyst attached to the pectoral muscle. Serial sections of the specimen proved it to be the larva of a tapeworm, and the finding of hooklets in some of the sections identified the organism as *Cysticercus cellulosae.*

Fig. 5 (case 3).—Cysticerci of abdominal subcutaneous tissue.

Laboratory Examinations.—An examination of the blood was not made.

The stool contained no ova of *Taenia.* Cysts of *Endameba histolytica* and ova of *Ascaris* were found.

CASE 5.—A Chinese military student, aged 27, came to the dermatologic clinic on March 29, 1929, for relief from small tumors underneath the skin. There were no local or constitutional symptoms. The patient denied eating uncooked or insufficiently cooked meats and had never noticed any segmented worm in his stools. He was not aware of a similar disease in his family or among his associates.

The first nodule appeared in the right subclavicular region three and one-half years before. Since then a few had appeared each year, the last two having been noticed about a month prior to admission, on the lower lip and leg. All of the

tumors were small in the beginning and had gradually increased in size. They never changed their positions.

On physical examination, a dozen freely movable, nontender subcutaneous nodules of hard rubbery consistency were located, chiefly on the trunk. There were three on the lower extremities, and one of particular interest situated beneath the mucous membrane of the lower lip near the right angle of the mouth. They varied from 0.3 to 1.5 cm. in size, the newer lesions being the smaller. A diagnosis of cysticercosis was made.

The eyes and the thoracic and abdominal organs were found to be normal.

Examination of Tumors.—One of the largest tumors in the right subclavicular region was chosen for biopsy. It was situated in the subcutaneous tissue and

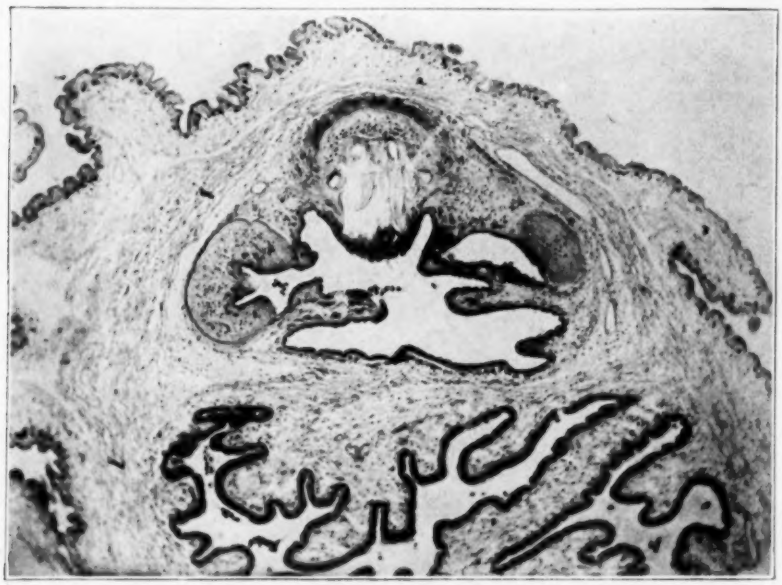

Fig. 6.—Section of *Cysticercus cellulosae* in cerebral cortex; × 90. Note the two hooklets near the top of the section.

measured 1.5 by 0.9 cm. On dissection, structures similar to those described in case 1 were found. The larva was identified by finding the rostellum and hooklets in the serial sections of a second cyst which was removed.

Skin Sensitization Test.—About 0.3 cc. of fresh serous fluid from a cyst was inoculated intradermally and by scarification into the arms of the patient. The only reaction was a little redness which appeared in the first few hours at the site of the subcutaneous injection. Observations were made at the end of half an hour, four, twenty-four and forty-eight hours following inoculation.

Laboratory Examinations.—The leukocyte count was 9,250, of which 72 per cent were polymorphonuclear neutrophils, 19 per cent lymphocytes, 5 per cent large monocytes, 3 per cent eosinophils, and 1 per cent basophils. The erythrocyte count was 5,224,000, with a hemoglobin content of 100 per cent (Hellige). The Wassermann and Kahn tests of the blood serum were negative.

The stools contained no ova or parasites.
The urine contained no albumin, sugar, casts or red blood corpuscles.

In the cases thus far described, lesions were manifest only in the subcutaneous and muscular tissues. In the following case, the central nervous system was the site of encystment.

CASE 6.—A Chinese medical student was seized repeatedly with epileptic convulsions. The finding of the larva with hooklets (fig. 6) in sections of the cheesy material removed at the time of operation established the diagnosis of cysticercosis cellulosae of the brain. There was no eosinophilia on several exami-

Summary of Clinical Observations in Six Cases of Cysticercosis Cellulosae

Case	Age and Sex	Occupation	Duration	Tissue Involved	Number and Distribution of Lesions	Stool	Sensitization Test
1	28 yr. Male	Farmer	1 yr., 1 mo.	Subcutaneous	50 in trunk and extremities	Positive for taenia ova and tapeworm	Negative
2	24 yr. Male	Student	12 yr.	Pectoral muscle	Solitary nodule in right pectoral muscle	Not examined	Not done
3	23 yr. Male	Military officer	1 yr.	Subcutaneous	12 in scalp, lower lip, trunk and arms	Negative	Not done
4	28 yr. Male	Military officer	1 yr.	Muscle and subcutaneous	80 in trunk, face and arms	Negative	Not done
5	27 yr. Male	Military officer	3½ yr.	Subcutaneous, submucous and muscle	22 in trunk and extremities, and mucous membrane of the lower lip	Negative	Negative
6	21 yr. Male	Student	4 mo.	Brain	Epileptic attacks; retinal hemorrhages and choked disks	Positive for taenia ova	Not done

nations. The ova of *Taenia* were repeatedly found in the patient's stools. Roentgenologic examination of his skull a year after the onset of epileptic fits revealed no calcified bodies.

Summary.—The accompanying table summarizes some of the clinical observations on these cases. All of the patients were young Chinese men between the ages of 21 and 28 years. Their occupations were of significance only in that they placed five of the patients in a social class that could afford meat with some frequency in its dietary. The one farmer was the single exception.

In each case, the final diagnosis was based on gross or microscopic examination of the cysticercal organisms removed from the living patient.

INCIDENCE

In the Peiping Union Medical College Hospital during a period of ten years, the six cases of cysticercosis cellulosae represent an incidence of approximately one case of cysticercosis in 25,000 patients. Similar statistics from other parts of China are not available for comparison.

During the same period, 143 cases of intestinal teniasis were observed, of which 49 were differentiated on the basis of examination of tapeworm segments. Of the 49 differentiated cases, 44 were due to *Taenia saginata* and 5 to *Taenia solium*. The high incidence of *Taenia saginata* is difficult to account for in a population which includes beef in its dietary much less often than pork. Reports of other investigators,[12] in various parts of China also show that teniasis saginata is more frequently encountered than teniasis solium. The relative frequency in man of the two species is approximately the same in other parts of the world. It is remarkable that not a single case of cysticercosis bovis was found among this group of cases in which the beef tapeworm constituted 90 per cent of the infestations. In Europe, the cysticercus of the ox has rarely been found in man. The diagnosis in such cases is uncertain, as it depends on the absence of hooks on the scolex of *Cysticercus bovis*, and occasionally these may be absent also in *Cysticercus cellulosae*.

Furthermore, it is worthy of note that of the five differentiated cases of intestinal teniasis solium seen in this hospital, two also manifested cysticercal lesions.

In view of the fact that five of the six patients were seen within the past two years, subcutaneous cysticercosis seems to be more frequently encountered here than in Western countries. This is to be expected in a country like China where sanitary laws have not been enacted and where intestinal parasitic infections are prevalent and uncontrolled. Many cases must have been overlooked for the simple reason that the cysts are usually small and, as a rule, do not disturb the hosts.

In other parts of the world, the disease varies considerably in frequency. It was formerly encountered rather often in German, Great Britain, France and Italy, but through enforcement of sanitary laws and the inspection of meat, the incidence has been remarkably reduced.[6] Cysticercosis is evidently rare in the United States and in Argentina. There are only a few cases on record involving the nervous tissues, and even the ocular form of the disease is rare, Ward[13] stating in 1918

12. Mills, R. G.: China M. J. **37**:932, 1923. Maxwell, J. L.: Research Committee, Fourth Interim Report, ibid. **24**:85, 1910.

13. Ward, H. B.: American Encyclopedia of Ophthalmology, 1918, vol. 5; quoted by Kress, G. H.: Am. J. Ophth. **7**:182, 1924.

that only 4 of about 400 cases reported throughout the world had been observed in the United States. The eighth case seen in Argentina was reported in 1922 by Mazza and Ivanissevich.[14] In this case, the masseter muscle was involved; in the other cases, the cysts were located in the eye or the brain. To 1927, only five cases had been observed at the University of the Philippines.[6]

DIAGNOSIS

So far as cysticercosis of the subcutaneous tissues is concerned, a probable diagnosis can be made without much difficulty, provided the condition is kept in mind. The tumors are easily confused with sebaceous cysts and fibromas, as may be seen in some of the cases here reported. Cysticerci can be differentiated from sebaceous cysts by the fact that the latter are usually attached to the overlying skin, whereas the former are, as a rule, freely movable, and can be rolled around like a foreign body under the skin. Fibromas are not so likely to be multiple and uniformly small; they are more a part of the surrounding tissues and are not so sharply circumscribed.

Besides direct examination of the cysts, laboratory evidence may throw some light on the diagnosis in certain cases. Eosinophilia frequently in itself indicates the presence of a parasitic infection. Hughes,[15] Priest [4] and Waterhouse [3] observed an increase of eosinophils in the blood of patients carrying *Cysticercus cellulosae,* which in some instances, was as high as 20 per cent. In none of our cases, however, was eosinophilia observed.

Roentgenologic examination may reveal the calcified cysts in the soft tissues,[16] but this is not often of diagnostic assistance. In case 2 and also in Douty's case,[17] calcification had not taken place for as long as twelve years after the appearance of the cysts.

Roth [18] reported a case in which multiple calcified lesions occurred in the muscles and subcutaneous tissue of both upper and lower extremities. In this patient, one calcified cyst had caused a chronic discharging sinus near the knee joint.

The finding of the ova of *Taenia* in the stools may be of considerable diagnostic significance in cases in which there are localizing signs

14. Mazza, S., and Ivanissevich, O.: Rev. Asoc. méd. argent. **35**:7, 1922; abstr., Cysticercus Cellulosa in Man, J. A. M. A. **79**:858 (Sept. 2) 1922.

15. Hughes, J. R.: Lancet **2**:956, 1921.

16. Pichler, K.: Wien. klin. Wchnschr. **24**:338 and 388, 1911. Roth, E. J. H.: Brit. M. J. **2**:471, 1926.

17. Douty, J. H.: Lancet **2**:69, 1886.

18. Roth (footnote 16, second reference).

or symptoms of a tumor. In case 6, the patient was suspected of having a cysticercus of the brain on the basis of infested stools. The presence of an encysted larva in the brain was later demonstrated at operation.

CUTANEOUS SENSITIZATION TESTS

In view of the analogy between *Cysticercus* and *Echinococcus* infection and the diagnostic value of sensitization tests in the latter disease,[19] we carried out similar skin tests on two of our patients (cases 1 and 5). Fresh fluid from a cyst was inoculated intradermally and by scarification into the arms. Observations were made within half an hour after inoculation and at the end of twenty-four and forty-eight hours. In both cases, the tests gave negative results.

MIGRATION OF CYSTS

Waterhouse,[3] among others,[1] believed that the cysticerci may move about under the skin after they have reached a size sufficient to be palpable or visible. Some of our patients were followed for several months, and in no case was there any evidence that the tumors had shifted their positions. It was observed, however, that some of the nodules, especially the smaller ones, were more easily felt at one time than another, depending on the state of contraction of the underlying muscles. Considering the consistency and size of the larva, one cannot believe that they could be palpated before encystment, and after encystment the enclosing fibrous sac is attached to the surrounding tissues in such a way as to make its movement for any signficant distance impossible.

TREATMENT

The eating of uncooked or poorly cooked pork must be avoided, especially in those countries where the infection of animals with *Cysticercus* is prevalent and where there are ineffective sanitary regulations or none for preventing or regulating the sale of infected meat.

Those persons who harbor the tapeworm in their intestines are liable to *Cysticercus* infection through the eating of self-contaminated food or as the result of regurgitation of ova into the stomach during the act of vomiting, as has been previously pointed out. It is essential that patients who have the cysticerci in their tissues be examined carefully for tapeworm, as its presence in certain cases must be responsible for the continuous appearance of new cysts. In any case, treatment of the intestinal teniasis is of the greatest importance both as a preventive measure against cysticercosis or as protection against occurrence of new lesions.

19. Rackemann, F. M., and Stevens, A. H.: J. Immunol. **13**:389, 1927.

Unless the presence of the cysts is of serious consequence to the patient there seems to be no good reason for their removal. When the lesions are in the subcutaneous tissues they can easily be excised, unless the number of them makes surgical removal unwarranted. Hughes [15] suggested the injection of 20 per cent carbolic acid in glycerin into the cysts when they are situated in the superficial tissues, and he reported that they disappeared within two or three days after this treatment. We found so much difficulty in the attempt to aspirate the contents of some of the cysts for use in performing skin tests that the practicability of this method of treatment seems doubtful to us.

SUMMARY

1. Six cases of cysticercosis cellulosae, five of the subcutaneous and muscular tissues, and one of the cerebral cortex, in Chinese patients in North China are reported. These were collected over a period of ten years and represent an incidence of about 1 in 25,000 patients.

2. In a series of 143 cases of intestinal teniasis, approximately 90 per cent of 49 differentiated cases were due to *Taenia saginata*. Of the remaining five cases in which *Taenia solium* was present, two also harbored *Cysticercus cellulosae*.

3. The characteristics of the cysts when they are located in subcutaneous tissue are such as to make their identification possible by physicial examination alone. They are as freely movable as a foreign body, of elastic hardness, nontender and, as a rule, are multiple and more or less uniformly small, the average being about 1 cm. in diameter.

4. Cutaneous sensitization tests performed on two of the patients with the fresh fluid from a cyst gave negative results.

COCCIDIOIDAL GRANULOMA

A CLINICAL AND EXPERIMENTAL REVIEW WITH CASE REPORTS*

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My object in this paper is to invite attention to results achieved from a clinical and experimental study of coccidioidal granuloma in experimental animals and in human beings, covering a period of three years. During this period, I observed, treated and studied nineteen patients suffering from this dreaded disease, and carried out some experimental work on guinea-pigs in connection with the probable mode of transmission. The preliminary results of this study, as based on the treatment of six patients of this series with colloidal copper and on the experimental work alluded to, were recorded in two consecutive communications which appeared in *California and Western Medicine* in 1927 [1] and 1928.[2] Since the publication of these articles, I have had the opportunity of further study of the disease in thirteen additional patients. The results of this study, together with an outline of the varying clinicopathologic picture of the disease, form the subjects of this communication.

Coccidioidal granuloma belongs in the class of infectious granulomas. Either its course may be exceedingly acute and end fatally in a few weeks, or the agony may be prolonged and a period of several years may elapse before death. Between these two extremes, as might be expected, there is a subacute type which is neither rapidly fatal nor unduly prolonged in its course, but which is characterized by a definite and positive tendency to widespread dissemination, with remissions and relapses, and in which the sufferer lives from six months to two years. Clinically, the disease is protean in its manifestations, and, while frequently mimicking tuberculosis in its multiform clinical forms, may simulate other disease entities and constitute a confusing diagnostic problem.

Ophüls classified the disease into the following three clinical types: (1) primary cutaneous lesions and later generalization, (2) primary

* Submitted for publication, Aug. 27, 1929.

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1. Jacobson, H. P.: Granuloma Coccidioides, Apparently Successfully Treated with Colloidal Copper, California & West. Med. **27**:360 (Sept.) 1927.

2. Jacobson, H. P.: Coccidioidal Granuloma, California & West. Med. **29**: 392 (Dec.) 1928.

pulmonary lesions and later generalization but no skin lesions and (3) primary pulmonary lesions and secondary subcutaneous lesions. To these I shall add three other clinical types which have come to my attention during the past year, and the details of which will be given later in this communication: (4) primary pelvic involvement without any skin lesions, (5) primary meningeal (spinal) involvement without any cutaneous or other lesions and (6) primary involvement of the bones, with secondary skin lesions.

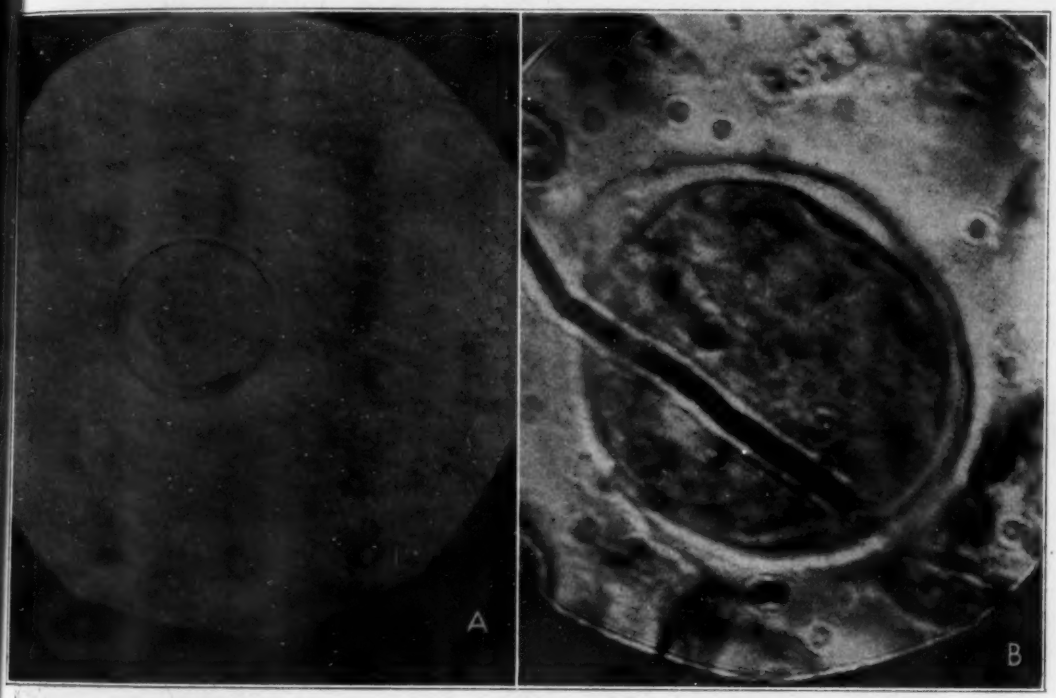

Fig. 1.—*A*, Coccidioides immitis in pus preparation under high microscopic magnification; *B*, Coccidioides immitis in stained tissue preparation under high microscopic magnification showing organism containing typical endospores and what appears to be a hypha originating from the capsule walls and ending in a conidia; endospores free in the tissue.

CUTANEOUS INVOLVEMENT

The cutaneous and subcutaneous lesions met with in coccidioidal granuloma are of several varieties which may be described as follows:

1. Dermic lesions: These lesions, which are nodular ulcerative, have their origin in the cutis or in the epidermic layers. From there, by continuity of tissue, the disease process may, and frequently does, extend to the subcutaneous tissues. Clinically, the lesions manifest them-

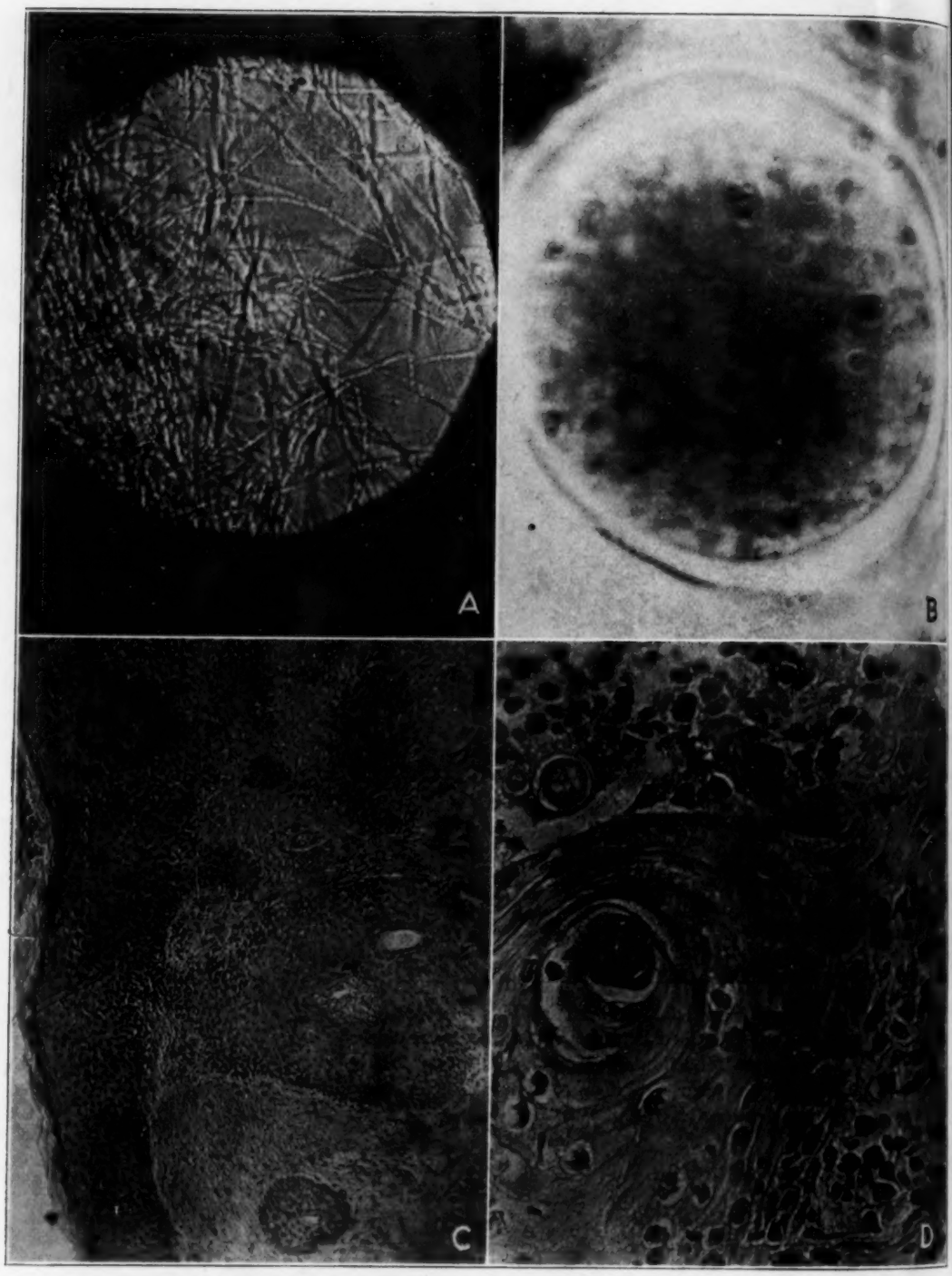

Fig. 2.—*A*, mycelial growth of organism on Sabouraud's medium; *B*, Coccidioides immitis in stained tissue preparation, reduced from a magnification of × 4600; *C*, low power study of skin section showing acanthetic and edematous epidermic changes and granulomatous reaction on the cutis, especially in the upper and middle layers; *D*, high power study of a skin section, showing epithelial whorls and anaplastic and hyperplastic epidermic involvement.

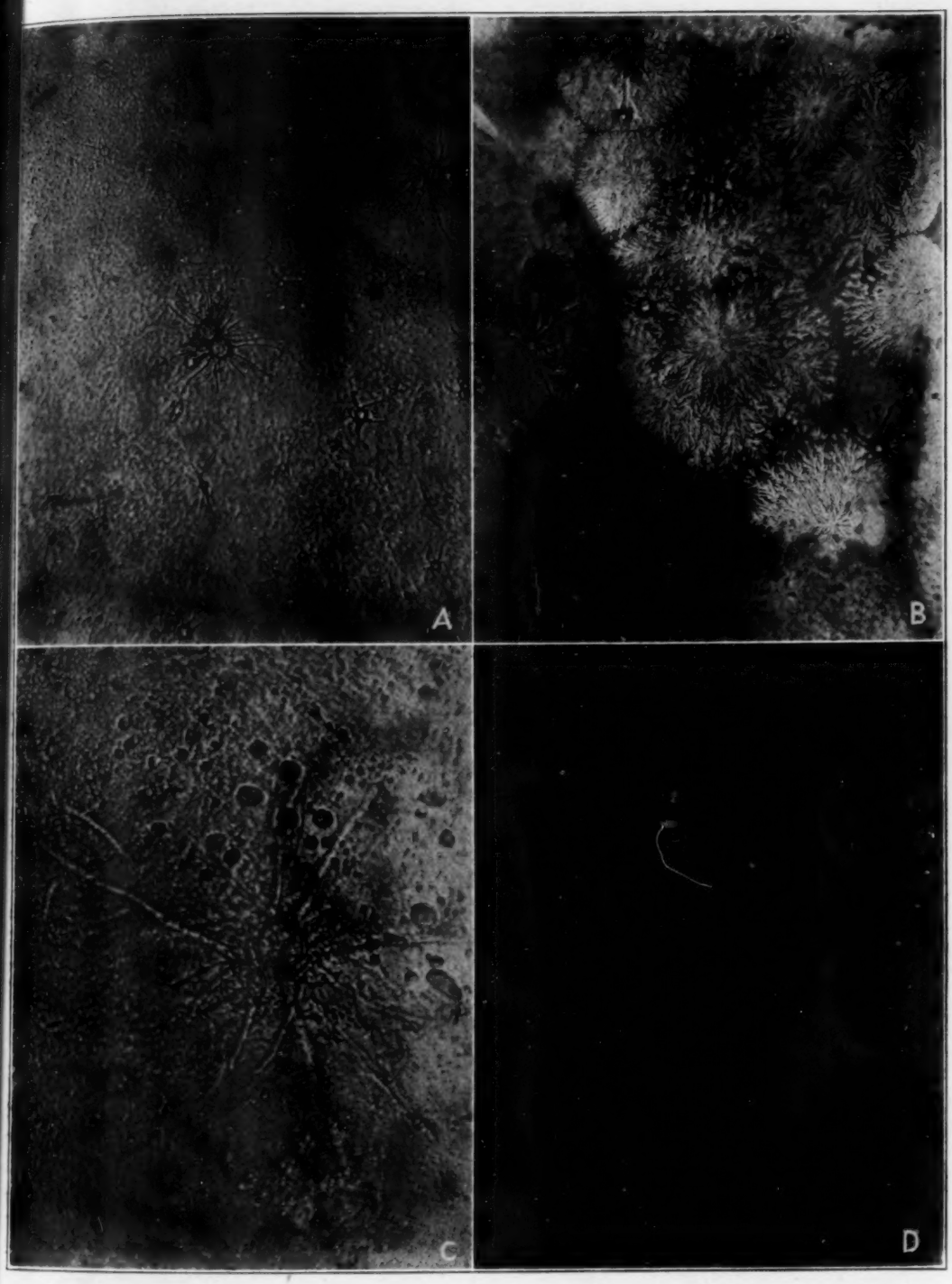

Fig. 3.—*A*, pus hanging drop — twenty-four hours' preparation on artificial medium under low power; note the origin of mycelia from the spore capsule; *B*, forty-eight hours' study of the same preparation; *C*, ninety-six hours' study of the same preparation; *D*, five days' study of a different field of the preparation shown in *C*.

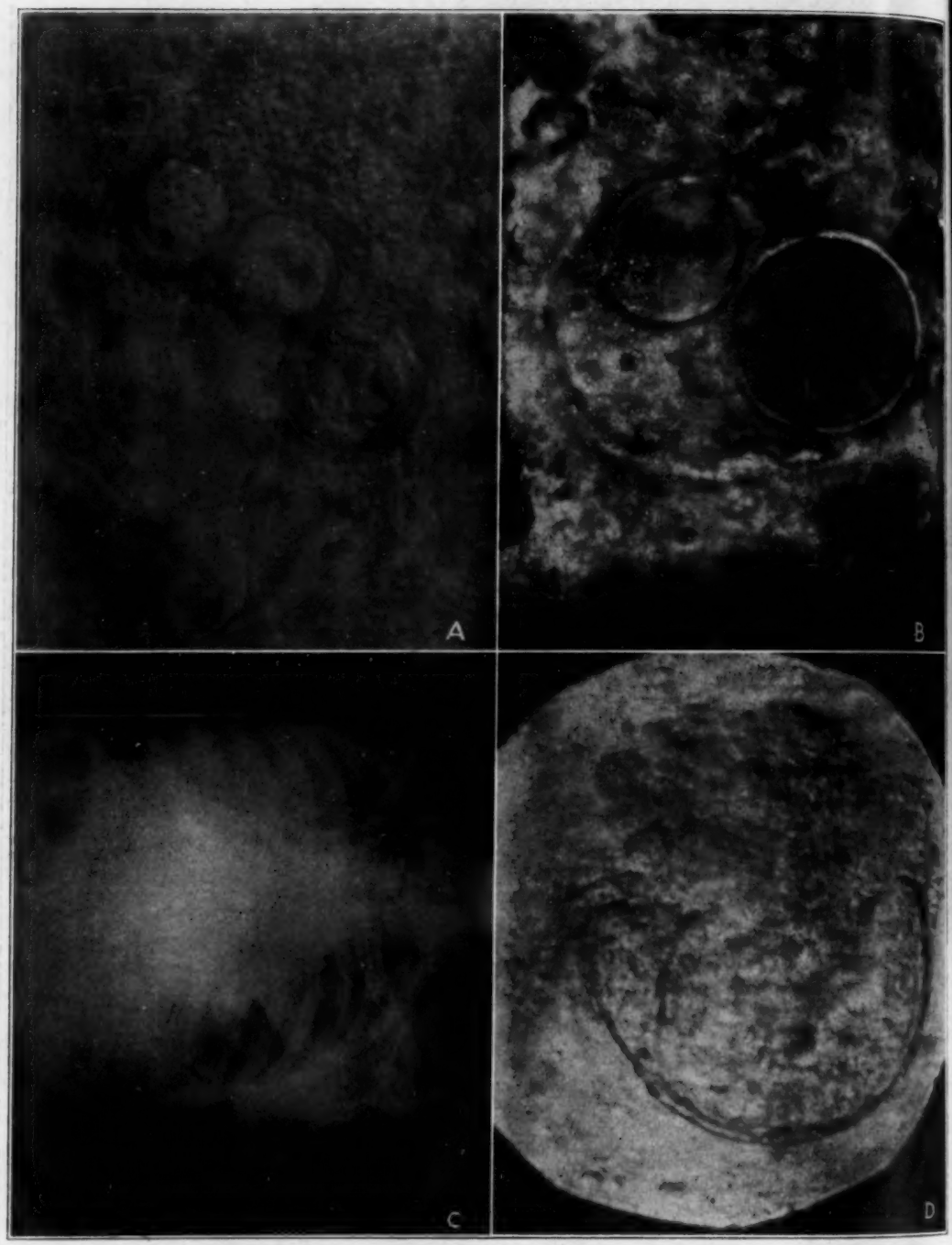

Fig. 4.—*A*, Coccidioides immitis in hanging drop pus preparation (six days); *B*, Coccidioides immitis is ascus (two organisms) in tissue; *C*, extensive pneumonic miliary coccidioidal involvement; *D*, rupture of capsule of Coccidioides immitis in pus preparation (high power).

selves primarily on the exposed portions of the body (the face, neck and distal portions of the upper and lower extremities) in the form of painless, deep-seated, pinkish to dusky red, solid nodules, of various sizes and shapes, which, after attaining a certain maximum size, ulcerate and exude a mucoid, grayish-yellow, fairly thick pus in which *Coccidioides immitis* may be found. The ulcers are necrotic and extremely sluggish. After a longer or shorter period, they may become papillomatous and resemble fungating epitheliomas. Under treatment, however, and occasionally without treatment, resorption and cicatrization may take place, leaving depressed, atrophic and fairly pliable scars.

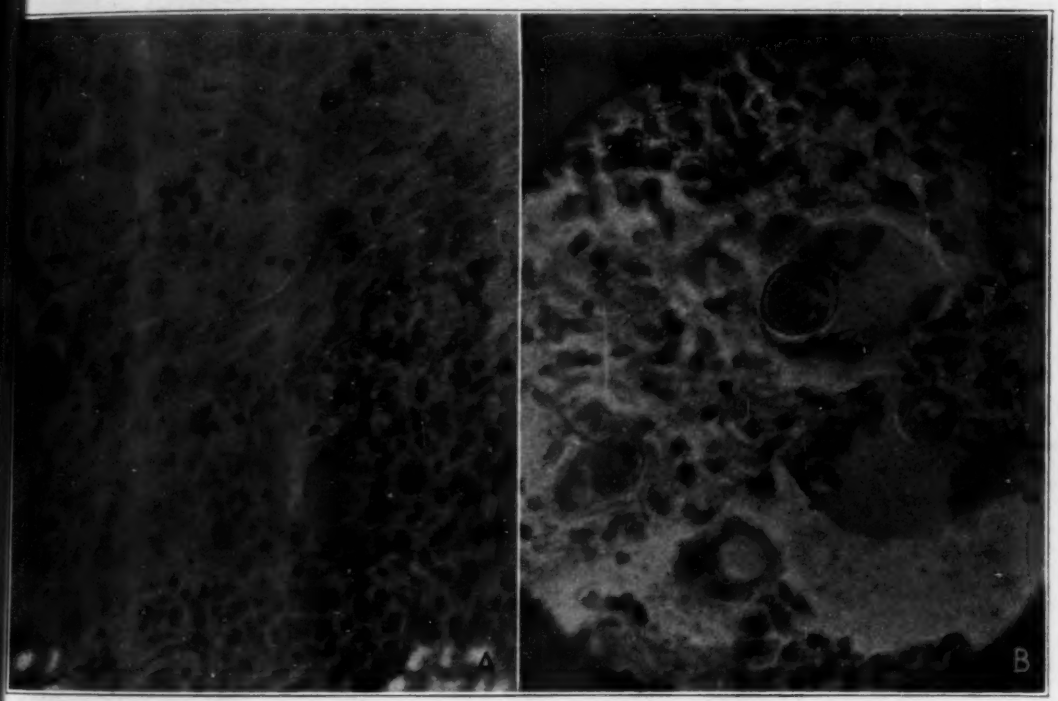

Fig. 5.—*A*, a number of organisms within the granulation tissue; *B*, giant cells containing Coccidioides immitis, some of which also lie loosely in the granulation tissue (high power).

2. Subcutaneous lesions: Subcutaneous coccidioidal involvement results in three types of lesions—the flaccid tumor, the abscess and the gummatous types.

The flaccid tumor lesions appear as soft, elastic, skin-colored, painless but frequently tender tumor masses of various sizes and shapes, which may be situated anywhere on the body. The tumors have their origin in the subcutaneous layers of tissue as cellular infiltrations, in response

to the presence of *Coccidioides immitis* and its toxins, and from there the infiltrating process extends upward toward the cutis. While they frequently attain large dimensions, these tumor masses seldom ulcerate or suppurate. There is usually no visible inflammatory reaction present, either of the skin covering of these elastic tumors or of the surrounding skin.

The suppurating or abscess lesions, like the former, have their origin in the subcutaneous layers of tissue anywhere on the body; the extremities are the parts most frequently involved. According to Ophüls, the abscesses are caused by the sporulating organism, whereas the solid

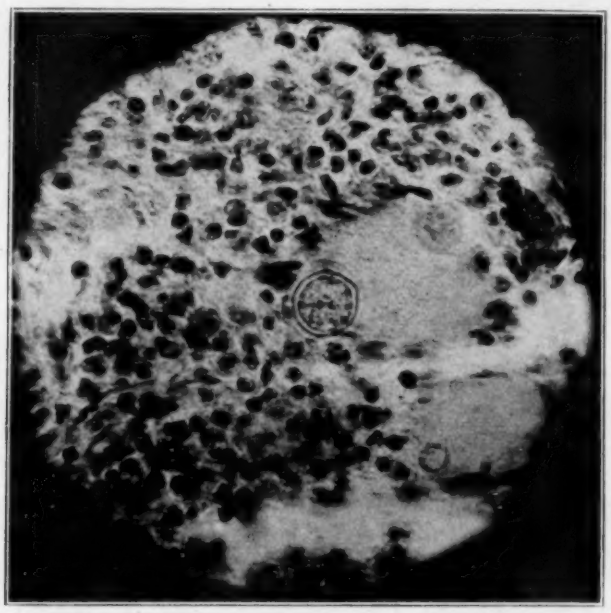

Fig. 6.—Showing the cytology of coccidioidal pathology and the organisms within giant cells (medium magnification).

tumor-like lesions described are caused by the mature, fully developed organism. Clinically, they manifest themselves in the form of abscesses of various sizes and shapes, without any visible inflammatory reaction of the skin covering or surrounding them, except in the presence of secondary infection. These abscesses, like the former lesions, frequently attain large dimensions and contain large quantities of fairly thick, mucoid, yellowish-gray pus, which harbors *Coccidioides immitis*. When situated near joints they cause a good deal of discomfort and pain which may be somewhat relieved by aspiration and evacuation of the pus. If left alone, the abscesses will sooner or later break through the skin and establish draining sinuses. Frequently the roof of the abscess which

is formed by the skin covering is destroyed by the suppurative process, leaving a larger or smaller ulcerated lesion.

The gummatous lesions, like the two preceding types, have their origin in the subcutaneous tissues. Clinically, they differ from the flaccid tumor and abscess types in their inflammatory and gummatous character with or without the presence of sinuses. Spontaneous resorption and cicatrization may occur.

Fig. 7.—*A*, flaccid tumor type of coccidioidal lesions on the face; *B*, scrofulodermic coccidioidal lesions; *C*, ulcerated coccidioidal nodular lesion of the nose with papillomatous degeneration resembling epithelioma; *D*, coccidioidal nodular ulcerative lesion on the chin in a patient with extensive pulmonary and meningeal coccidioidal involvement.

3. The scrofulodermic type of lesion: This type has its origin in the superficial lymph glands of the body, most frequently in the supraclavicular region and other parts of the neck. The pathologic process and the clinical picture are quite analogous to those which obtain in some of the other infectious granulomas, such as tuberculosis, syphilis,

sporotrichosis, etc. The involved lymph glands, because of the specific inflammatory process, present themselves at first as firm, well defined, subcutaneous nodules which gradually enlarge, become attached to the overlying skin and subsequently degenerate to form ulcers on the surface of the skin, and which may terminate in resorption and cicatrix formation, or the process may continue and extend to adjacent structures.

PATHOLOGIC HISTOLOGY

The pathologic histology of these lesions is similar to that observed in tuberculosis and in some of the other granulomas. In the nodular ulcerative type, the pathologic process may have its primary seat either

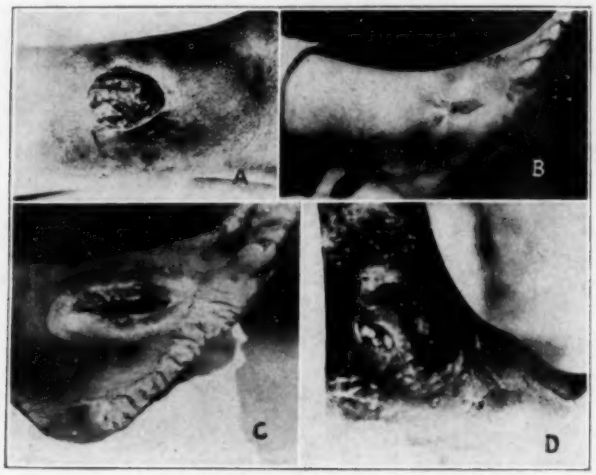

Fig. 8.—*A*, isolated coccidioidal shallow ulcerated lesion of the thigh (resulting from a coccidioidal abscess) in a patient, aged 15 years; *B*, healed coccidioidal lesion, following treatment with colloidal copper and coccidioidin-B; *C*, broken-down coccidioidal gummatous lesion, and *D*, gaping necrotic lesion of the ankle and foot following operation for osteomyelitis which proved to be of coccidioidal etiology.

in the corium or in the epidermic layers, with subsequent involvement of the subcutaneous tissues by extension of the process downward. In the subcutaneous and scrofulodermic types, the primary seat of the lesion is either in the subcutaneous layers or in the lymph glands with subsequent dermic involvement by extension of the process upward.

In either event, the histopathologic process is essentially the same and consists of a marked parenchymatous and interstitial edema of the tissues of the corium and subcutaneous layers, accompanied by cellular degeneration of various kinds, new blood vessel formation, and a diffuse cellular infiltration throughout the involved tissues. The cellular infiltrate is composed of lymphocytes, epithelioid and giant cells (usually

of the Langhans type), with an occasional plasma cell and now and then a polymorphonuclear leukocyte. Tubercle formation and caseation necrosis are frequently present. *Coccidioides immitis* is usually engulfed in the giant cells, as many as from five to eight organisms being found within one giant cell. Somewhat less frequently the organism may be found embedded in the granulomatous tissue, outside of the giant cells.

The unbroken epidermis is usually irregularly acanthotic and involved in a generalized parenchymatous and interstitial edema, with some vesiculation but seldom any definite abscess formation, as is observed in cutaneous blastomycosis. Epithelial whorls and hyperplastic and anaplastic changes of all the epidermic layers may be observed in the nodular papillomatous type of lesions.

Fig. 9.—Large abscess-like coccidioidal lesion.

PREVALENCE

Since the first published report of the existence of this disease appeared,[3] a total of ninety-five instances of the infection have been reported from time to time by different clinicians in various parts of the world. About 80 per cent of the patients in these case reports gave histories of residence in California, for the most part in the San Joaquin valley. Some contracted the disease while residing there; others, however, began to have symptoms of the malady months or years after leaving that state. The remaining 20 per cent of patients in this series never lived or visited California, but contracted the disease while living in one of the following states and countries: Arizona, New Mexico, Texas, Illinois, Kansas, Missouri, Pennsylvania, South Carolina, Washington, Mexico, Argentine, Brazil and Canada.

Because of the foregoing facts, the impression has become prevalent that coccidioidal granuloma is a rare disease and that the habitat of

3. Wernick, Robert: Centralbl. f. Bakteriol., 1892, vol. 12. Posadas, A.: Rev. de chir., 1900, p. 276.

Coccidioides immitis is almost exclusively confined to the boundaries of California, with the result that "California disease" has become the synonym of coccidioidal granuloma.

That this impression has no basis in fact will be conceded by every student of the subject. Frequently the persons with this malady present clinical pictures closely simulating pulmonary or miliary tuberculosis. The correct diagnosis in these cases is occasionally established post mortem if the pathologist happens to be familiar with the similarity of these two conditions and is not satisfied with macroscopic appearance only but makes a micropathologic study in addition. In the last few months, several instances of this sort came to my attention. One of these patients was an infant, aged 3 months, who was brought to the

Fig. 10.—*A*, acute fulminating coccidioidal infection with extensive visceral involvement and cutaneous lesions; *B*, ulcerative gummatous lesions of the skin with destruction of the sixth and seventh ribs and intrapleural abscess in a child, aged 3½ years.

Los Angeles General Hospital with a diagnosis of pneumonia and acute respiratory difficulty due to the pressure of tuberculous glands. Death occurred three hours after arrival at the hospital. Autopsy revealed cervical adenopathy and abscess formation, caused by *Coccidioides immitis*.

Unfortunately, however, not all cases erroneously diagnosed ante mortem as tuberculosis reach the autopsy pathologist. Reasoning from the known to the unknown, it is fair to suppose that, because of the prevailing opinion that coccidioidal granuloma is essentially a disease of California and therefore seldom thought of outside of the borders of that state, there must be other patients with coccidioidal granuloma

who are making the rounds of thoracic and orthopedic surgeons and clinics of the country without arousing any suspicion that *Coccidioides immitis* is the offending organism; else how could one account, for instance, for the isolated occurrences of this infection in some of the states enumerated? Certainly, it is hard to conceive how an organism like *Coccidioides immitis,* which thrives so luxuriantly in animal tissues and which apparently finds the human economy a most excellent environment for its nutrition and propagation, would willingly confine its activities in such large centers of population as Texas, Illinois, Missouri, etc., to one or two persons, without manifesting any further evidence of its existence there in the course of years.

Nor is tuberculosis the only disease which coccidioidal granuloma is capable of mimicking. Several months ago, for instance, a female

Fig 11.—Cutaneous allergic reaction to coccidioidin-A with control reaction below.

patient was admitted to the neurologic service of this hospital for a condition which was diagnosed as a neoplasm of the lumbosacral cord. Operation, sectioning and microscopic study of the tissue of the supposed neoplasm secured at the operation, resulted in the finding of *Coccidioides immitis.* (Dr. Carl Rand, the neurologic surgeon who operated on the patient, recently had a similar case with involvement of the cervical cord.)

In the light of the foregoing observations it seems reasonable to deduce, therefore, that coccidioidal granuloma is probably a widely prevalent disease and not confined geographically within the borders of California. Bearing in mind its protean character, one should think of it in all obscure conditions and in all parts of the country. Moreover, a single negative microscopic or cultural observation should not constitute a definite case against coccidioidal infection. Often, in the presence of secondary pyogenic bacterial infection, repeated smears and cultures

may be required before a successful growth is obtained or before microscopic examination reveals the presence of the organism. Furthermore, there seem to be many strains of the organism with varying capacities for growth on artificial mediums and apparently capable of expressing themselves clinically in the different types of the disease enumerated. Diligent and persistent search, however, even in the presence of secondary infection, will always result in the finding of the organism in the pus or in the tissue secured by means of biopsy on an accessible lesion. When the infection, however, is of the primary visceral type, and there is no opportunity for study of the tissue or pus, the cutaneous allergic test described in a previous communication [4] should be resorted to; it often gives gratifying results.

Fig. 12.—Allergic cutaneous reaction to coccidioidin-A, in an experimentally infected guinea-pig.

ETIOLOGY

The etiologic agent of the disease is *Coccidioides immitis,* a vegetable fungus of the general class of fungi imperfecti. Botanically, the position of this organism is as yet unsettled; some authorities class it with the hyphomycetes, while others prefer to group it with the ascomycetes. It is pathogenic for dogs, guinea-pigs, rabbits and probably sheep and cattle, animals in which it is capable of producing lesions similar to those which are encountered in human beings. Until recently there has been some confusion as to its relationship to the blastomyces, but today it is fairly well conceded that the two organisms are separate and distinct.

4. Jacobson, H. P.: Coccidioidal Granuloma; Specific Allergic Cutaneous Reaction; Experimental and Clinical Investigations, Arch. Dermat. & Syph. **18**: 562 (Oct.) 1928.

Coccidioides immitis has a double cycle of growth, without any features in common, one in the tissues and one on artificial culture mediums. In the tissues and in the pus the organism exists as a double-contoured sphere, varying in size from 5 to 60 microns and containing a granular protoplasm. Under sufficiently high microscopic magnification, some of these granules are seen to be replicas of the parent organism, consisting, like the latter, of a central, deeply staining mass of protoplasm enveloped by a spherical, double-contoured capsule. In the tissues of infected animals and human beings, the organisms are seen within the giant cells or situated loosely in the granulation tissue; frequently there are from six to ten organisms in a single field. Two organisms within an ascus were recently observed by Dr. E. S. Miller and me in a tissue section.

Reproduction in the tissues and in pus is accomplished by means of endosporulation, though Dr. Miller and I have noted evidence of budding in some of our preparations of pus.

When grown artificially, on dextrose agar medium (best at incubation temperature, though some strains thrive well at room temperature), growth appears in from twenty-four hours to ten days, depending on the virulence of the organism, in the form of small, paraffin-like, elevated, round plaques; these soon become covered and surrounded by fluffy, snowlike flakes which sooner or later penetrate deeply into the medium and turn brown with age. In broth they grow as fluffy, mucoid masses which sink to the bottom.

Microscopically, the growth appears as an intricate mycelial network with long, branched, septate hyphae with the formation of chlamydospores and conidia in older cultures.

SOURCE OF INFECTION AND MODE OF TRANSMISSION

The question of the source of this infection and the manner of its transmission has been puzzling students of this problem ever since the disease was first recognized as a clinical entity. Ophüls,[5] the first investigator to express an opinion, suggested that the disease was originally a disease of animals and was only occasionally transmitted to man. In the same article, he also expressed the opinion that the atrium of infection may be primarily the respiratory tract or the skin. Soil and vegetation have also been suggested as possible sources of this infection, because many of these patients have had outdoor occupations, such as picking grapes or walnuts, working with cement, etc. M. Dorothy

5. Ophüls, W.: Further Observations on a Pathogenic Mould Formerly Described as a Protozoon (Coccidioides Immitis, Coccidioides Pyogenic), J. Exper. Med. **6**:444 (Feb. 4) 1905.

Beck,[6] from the California State Department of Public Health, reported finding coccidioidal lesions in the upper respiratory tract in seven slaughtered cattle and sheep coming from widely separated geographic locations, and concluded that both man and animals are infected from the same source. Florence E. Ahlfeldt[7] succeeded partially in transmitting the disease to experimental animals by means of contaminated food and air as well as by rubbing the dry mold into abraded skin or oral mucous membrane, and by injecting the dry mold, in solution or suspension, into the trachea.

My own experimental and clinical observations in connection with this phase of the problem have been recorded in *California and Western Medicine*.[2] It may not be amiss, however, to restate here that experimental attempts to transmit the disease from guinea-pig to guinea-pig, by means of contaminated food and air and through intimate contact between infected and control pigs, proved to have totally negative results. These results, coupled with significant clinical facts—(*a*) no known case of transmitted infection from man to man; (*b*) the usual involvement of exposed portions of body; (*c*) the occasional history of insect bite preceding the onset of the disease; (*d*) the victims being usually of the poor industrial class, living in an unhygienic environment which gives excellent opportunities for the breeding of all sorts of insects—lead me again to express the view that the unknown factor in the transmission of the disease is an insect of some sort, feeding either on contaminated soil, vegetation or infected rodents and transmitting the infection to animal and man by means of a sting and deposition of *Coccidioides immitis* in the injured skin or mucous membrane in which the disease process begins.

TREATMENT

The treatment for coccidioides has been a matter of much concern to the medical profession. Because of the seriousness of the condition, clinicians and experimental investigators of the problem have turned their attention toward the discovery of a method of treatment which would effectually check the progress of the disease and alleviate the suffering of the victims. Accordingly, a number of remedies that have proved successful in the management of other diseases have been employed from time to time in the treatment for this infection by various clinicians in different parts of the country. Among these methods may

6. Beck, M. Dorothy: Occurrence of Coccidioides Immitis in Lesions of Slaughtered Animal, Proc. Soc. Exper. Biol. & Med. **26**:534 (March) 1929.

7. Ahlfeldt, Florence E.: Studies in Coccidioidal Granuloma: Mode of Infection, Arch. Path. **2**:206 (Aug.) 1926.

be mentioned roentgen rays, surgery, iodides, and intravenous injection of crystal violet, gentian violet, arsphenamines and tartar emetic. The results obtained from these methods of treatment, as the records will show, have been eminently unsatisfactory. A few apparent recoveries have been achieved by means of the amputation of extremities when the disease process was localized and confined to them, and by means of roentgen rays in conjunction with the intravenous injection of tartar emetic.[8] The available records also show that all other reported cases have terminated fatally. In view of these discouraging observations, the results achieved in the treatment of this disease by means of colloidal copper and coccidioidin-B are rather encouraging, to say the least. Of a series of fifteen patients treated in three and one-half years, only four are known to have succumbed to the disease; two are in the hospital and bedridden though definitely improving, and five are ambulatory and economically self-sufficient. One of these is working as a domestic and is coming for treatment irregularly; another refused further treatment, though his condition required it, while three others feel too well to submit to further treatment. The remainder of this series have left Los Angeles, and their present status is unknown. It is reasonable to presume, however, that in view of the relief they obtained from treatment, they would probably return for further treatment if their present condition demanded it. On the other hand, assuming for the sake of scientific conservatism that the patients who left my jurisdiction have all succumbed to the ravages of the disease there still remain six of a total of fifteen patients, five of whom have, as a result of treatment, sufficiently recovered to be economically self-supporting, while one patient with a generalized and extensive involvement of bones and joints, is still at the hospital and shows definite evidence of improvement.

The method of treatment employed has its limitations, of course; it is neither specific nor 100 per cent efficacious. It makes no impression, for instance, on the acute fulminating type of the disease which is obviously due to an extremely virulent organism with probably an associated markedly reduced resistance of the patient. (In this connection, I wish to make the observation that all those patients under my care who exhibited cutaneous lesions of the face have had the serious and fatal type of the disease, while none of those suffering from the milder type of the disease presented lesions of the face.) In the subacute and chronic form of the disease, however, the method of treatment has much in its favor and may be employed with a good deal of promise to the patient and a great degree of satisfaction to the attending physician.

8. Guy, W. H., and Jacobs, F. M.: Granuloma Coccidioides, Arch. Dermat. & Syph. **16**:308 (Sept.) 1927.

TECHNIC

The technic of the treatment is simple. Deeply in the gluteal region the patients are given injections of colloidal copper from every four to seven days, depending on the degree of systemic reaction. In addition, coccidioidin-B (exotoxin and endotoxin) is injected cutaneously, from every eight to fourteen days, also depending on the degree of the local and constitutional reaction. In certain selected cases, carbon dioxide snow may be applied to isolated cutaneous lesions without pressure for a period of from five to eight hours through a heavy layer of petrolatum. In the systemic type of the disease, rest, proper food, air and other hygienic measures must, of course, be accorded the same degree of consideration as in other constitutional diseases.

REPORT OF CASES

Case 1.—A. V., a Mexican laborer, aged 21, was admitted to the orthopedic service of the Los Angeles General Hospital on Aug. 5, 1928, with a diagnosis of osteomyelitis of the right foot. The condition commenced some time in February, 1928, with a sore and red area on the dorsolateral aspect of the foot, which gradually became tender and painful and formed a small "boil." The boil soon opened and began to discharge pus; nearly the whole foot became dark red and painful, and the patient was forced to seek relief at the hospital. After a period of observation in the orthopedic service of the hospital, and based on roentgen and clinical study of the case, a diagnosis of osteomyelitis of the cuboid, fourth and fifth metatarsal and external cuneiform bones was made. The foot was operated on, on August 14. In the necrotic material obtained at this operation, *Coccidioides immitis* was found microscopically and culturally. The patient was then referred to my dermatologic service for treatment on August 26. Examination of the patient the next day revealed a markedly swollen foot, ankle and lower third of the right leg, and a vertical, necrotic, gaping wound of the anterior aspect of the leg to the dorsum of the foot, forming a large, crater-like cavity, the walls and floor of which were markedly necrotic and purulent; the surrounding skin was dusky red and gummatous. The constitutional symptoms consisted of a moderate rise in temperature and a disproportionately accelerated pulse rate and loss of weight. Roentgen examination at this time revealed a destructive process of the cuboid bone and the adjacent portion of the fifth and sixth metatarsal bones, with possible increased destruction since the roentgen examination on July 5. There was no evidence of proliferation or effort at repair. An intradermal injection of 0.3 cc. exotoxin (coccidioidin-A) into the skin of the forearm resulted in a characteristic local reaction in the course of twenty-four hours.

Treatment.—Treatment with colloidal copper and coccidioidin-B was begun immediately and resulted in a gradual but steady improvement, both local and constitutional. The patient was discharged from the hospital on September 29. He has since been coming to my office for observation and treatment, and to all appearances the disease process is definitely checked though he is still receiving treatment. He is working again as a laborer and is economically self-sufficient. A roentgen examination on Jan. 10, 1929, revealed no advancement of the destructive process as compared with previous roentgen studies, but rather a more sharply cut involvement and evidence of an attempt at repair. The final outcome is uncertain.

Case 2.—A. H., a colored girl, aged 7 years, was admitted to the Los Angeles General Hospital in April, 1928, complaining of pain in the shoulder joint and right knee, and an afternoon fever.

History.—The illness had its onset about three months before admission to the hospital, but did not incapacitate the patient until two weeks before, when her right knee became markedly swollen and painful and she was unable to walk. A physician was consulted; after aspirating some fluid from the swelling, he informed the family that the patient had tuberculosis of the bones. Two weeks later, she was admitted to the Los Angeles General Hospital.

Examination at the time of admission revealed an emaciated colored child who complained of a painful knee and shoulder and was apparently uncomfortable. There was marked cervical adenopathy and rather large infected tonsils. Examination of the chest revealed numerous râles and other evidence of pulmonary involvement. In the region of the right tibial tuberosity, there was a walnut-sized fluctuating tumor mass, which was painful. The right shoulder joint also was painful. Roentgen examination of the chest and shoulder on April 16 gave essentially negative results. Roentgen study of the knee, however, revealed a sharply circumscribed destructive lesion with little proliferative reaction, centering at the tibial tuberosity. Pus which was aspirated from below the right knee was positive for *Coccidioides immitis,* culturally and microscopically.

On April 31, she was transferred to my dermatologic service for treatment. Examination at this time revealed, in addition to the foregoing observations, a draining sinus of the upper third of the right leg, and a hypertrophic, painful protrusion of the first thoracic vertebra. A painful and tender gummatous mass involved the right ankle. A draining sinus on the lower third of the inner aspect of the right tibia appeared later. The patient coughed considerably and complained of pain on the slightest movement. A roentgen report, on April 23, stated that there was a destructive process of the first and second dorsal vertebrae with cold abscesses; also a destructive process in the lateral aspect of the epiphysis of the right radius, extending forward to the anterior portion of the joint. An intracutaneous injection of 0.3 cc. of coccidioidin-A resulted in a characteristic local reaction. Treatment with colloidal copper and coccidioidin-B was commenced soon after the patient was transferred to my service. At this writing, she is still at the hospital under my care, and is apparently holding her own. What the ultimate outcome will be, of course, is problematic, but the fact that she is still living in spite of the extensive and virulent infection is encouraging.

Case 3.—C. R., a Mexican boy, aged 15 years, was admitted to the Los Angeles General Hospital on March 13, 1928, because of a painful, ulcerated right thigh, a mild cough and fever. The present illness began about three weeks before with painful swelling which gradually enlarged, finally ruptured and commenced to discharge pus. In addition, he began to feel feverish and to cough.

Examination revealed a fairly well nourished Mexican boy who presented a sluggish, oval, fairly deep ulceration, about 10 by 7 cm. in size, on the anterior surface of the middle third of the right thigh. This lesion had been treated in another department of the hospital with local applications of mercurochrome-220 soluble in spite of which it continued to extend until he was transferred to my dermatologic service on April 7. Roentgen studies of the right femur on March 14 and April 3 revealed no involvement.

Roentgen studies of the chest revealed a fine nodulation in the greater part of the right lung, most of which appeared to be associated with the bronchial trunk, a special accentuation toward the apex and a soft circumscribed mass projecting from the right side of the mediastinum at the left aortic arch, the origin of which was not clear.

Laboratory Observations.—Direct microscopic examination of pus obtained from the ulceration, after several unsuccessful searches, revealed several spherical

bodies resembling, but not characteristic of, *Coccidioides immitis.* It took several attempts to grow the organism successfully on Saboraud's culture medium. (The explanation for this difficulty may perhaps be found in the presence of secondary pyogenic bacteria capable of inhibiting the growth of the fungi.) Microscopic study of tissue obtained by biopsy on the border of the ulcer disclosed numerous spherical bodies that were typical *Coccidioides immitis.* Intracutaneous injection of 0.3 cc. of coccidioidal filtrate (coccidioidin-A) resulted in a characteristic local cutaneous reaction. Treatment with colloidal copper and coccidioidin-B was commenced on April 24. Improvement began in about two weeks and continued steadily until the patient was discharged from the hospital in good condition on May 26.

Case 4.—M. M., a woman, aged 24, a Mexican domestic, was admitted to the Los Angeles General Hospital, Feb. 6, 1928, with a diagnosis of (1) acute salpingitis, (2) possible pelvic abscesses and (3) pelvic peritonitis.

History.—The patient had lived in Los Angeles all her life and had not been in good health since her marriage at the age of 15. She had had a vaginal discharge and pain in the lower part of the abdomen most of the time since shortly after her marriage, although she was unaware of any venereal disease in her husband. Five years before admission to the hospital, she was divorced from her husband, who was twenty-three years her senior, because he beat her and was generally cruel to her. Since that time, she had been promiscuous in her relations with men; she admitted that she had had intercourse with at least two different men at frequent intervals. One of these men had lived in Los Angeles during his entire life, and the other lived in Texas; so far as she knew, both were perfectly well. For the previous four and a half years she had been having pain in the right lower quadrant of the abdomen, chiefly an aching pain, with occasional acute attacks (at least once a year) of sharp, knifelike pains. On October 3, she became acutely ill. The aching pains in the lower part of the abdomen, which she described as a feeling "that something was stuffed in her lower abdomen," became so severe, especially when she attempted to walk, that her "limbs seemed almost paralyzed." She finally developed fever and became sufficiently ill to necessitate the services of a physician, who put her to bed and advised the application of ice caps to the lower part of the abdomen. She finally improved enough under that treatment to be able to return to work on December 7. On Feb. 5, 1928, she again became acutely ill with an onset of severe chills and alternate drenching sweats, fever and abdominal pain. On Feb. 6, 1928, she was admitted to the gynecologic service of the Los Angeles General Hospital; after an extended period of observation and expectant treatment, during which time she presented a clinical picture of massed pelvis, she was finally operated on, on March 21, 1928.

Observations at Operation.—Dense and extensive adhesions were found between the pelvic organs and loops of the small intestine, with many acute angulations of the latter. All these structures were adherent high on the abdominal wall, so that it was necessary to extend the incision to the side of the umbilicus in order to enter the peritoneal cavity. Both tubes and the right ovary were destroyed by the inflammatory process, and the broad ligaments were extensively infiltrated. The adhesions were freed with the greatest difficulty, and in doing so, an opening was made in the lumen of the small intestine. This was closed with two layers of sutures of no. 0 chromic gut. Both tubes and the right ovary were removed. The raw surfaces of the abdomen were closed, one rubber drain was put in the culdesac, and the operation was completed in the usual fashion.

Pathologic Report.—Nine slides of the ovary, both tubes and the omentum showed coccidioidal granuloma. The general appearance was similar to that of tuberculosis, and there were large numbers of giant cells, some discrete and others surrounded by epithelioid cells and lymphocytes as in a tubercle. The coccidioidal organisms were numerous; they were often within the giant cells or free in the inflammatory tissue. They were doubly contoured and variable in size, and frequently contained numerous endospores.

Roentgen Report.—Roentgenograms of the chest, on April 2, showed the diaphragm high on both sides. The pulmonary condition was essentially clear, except for some questionable thickening in the right perihilar region toward the base and not extending to the periphery. This was indefinitely nodular, and the pulmonary shadows were somewhat hazy and nodular throughout.

The patient was transferred to my service on April 17, after the diagnosis of pelvic coccidioidal granuloma was established microscopically. Examination on that date revealed a large draining sinus in the abdominal wound, with no apparent tendency to heal. There was a low grade fever and a disproportionately rapid pulse. The pus from the sinus was examined culturally and microscopically, and revealed *Coccidioides immitis.* The intracutaneous injection of 0.3 cc. of exotoxin (coccidioidin-A) resulted in a characteristic local reaction in twenty-four hours. Treatment with colloidal copper and coccidioidin was commenced at once and resulted in the prompt and favorable response of the patient. She left the hospital on May 30 in a good condition generally; the wound was completely healed. She continued to receive ambulatory treatment for about two months, and then refused further treatment because she felt perfectly well. On March 5, 1929, she again appeared at the county hospital with a complaint of pain and soreness in the right lower side of the abdomen. An examination by Dr. Lettice, who operated on her, revealed a pelvic mass on that side. She was then referred back to my service, and treatment with colloidal copper and coccidioidin-B was immediately commenced; she is responding well.

Case 5.—O. R., a Mexican laborer, aged 53, arrived in Los Angeles during the early part of 1925, where he lived and worked continuously until he was admitted to the Los Angeles General Hospital on April 2, 1928. His present illness had its inception thirteen months before, with a swelling on the outer side of the right ankle. The swelling gradually enlarged and became darker. In the course of several months a number of similar but smaller swellings appeared, and the ankle and foot became tender and painful. A year after the onset of his illness, the patient became sufficiently alarmed to seek medical advice.

Examination revealed marked swelling of the lower third of the right leg, ankle and dorsum of the foot; the overlying skin was stretched and dusky red. In places, the involved extremity presented fluctuating foci with here and there a sinus that drained a yellowish-gray, tenacious, purulent material. Motion of the ankle joint was somewhat limited.

Roentgen studies on April 4, 1928, revealed a destructive process over the external malleolus and a periosteal reaction on all aspects of the shaft of the fibula. There were marked changes in the soft tissues of this region. A roentgenogram of the chest, on April 18, disclosed a fine nodular infiltration disseminated throughout both lungs; it was more advanced toward the clavicle and was associated with only moderate hilar thickening. The appearance was consistent with disseminating pulmonary tuberculosis that approached the miliary type.

Laboratory Observations.—Examination of the pus obtained from the open sinuses revealed *Coccidioides immitis* culturally and microscopically. Intra-

cutaneous injections of 0.3 cc. coccidioidal filtrate (coccidioidin-A) resulted in a characteristic cutaneous reaction.

Treatment.—Treatment with colloidal copper and coccidioidin resulted in a gradual but steady improvement. The patient was discharged from the hospital in good condition, on May 26, 1928.

Case 6.—B. C., a Mexican housewife, aged 28, was born in Mexico and lived there until twelve years ago, when she moved to California. She was admitted to the Los Angeles General Hospital on July 6, 1928, for her present illness, which began six months before with a swelling on the right side of the face in the malar region. Soon thereafter, similar swellings appeared on the right side of the chest, breast, forearm and foot; these compelled her to go to bed. In the course of a few weeks the swellings ruptured and began to drain pus; two and one-half months after the onset of the illness, most of the joints, large and small, began to swell and became tender and painful. Side by side with the development of the local symptoms, her general health began to decline. Evidence of constitutional involvement, such as a severe cough, profuse perspiration, rapid loss of weight, etc., became manifest. These signs and symptoms gradually but progressively grew worse and finally resulted in her coming to the hospital.

Examination at this time revealed an emaciated Mexican woman, who looked much older than she was, and who was obviously ill and in marked discomfort. There were numerous, variously sized, fluctuating and gummatous masses and draining sinuses in different parts of the body, involving the face, trunk and extremities. The joints of the upper and lower extremities, especially the large ones on the right side of the body, were all markedly swollen, fluctuating, tender and painful, and drained purulent material. *Coccidioides immitis* was easily recovered from the drained material, both culturally and microscopically.

Roentgen studies revealed various destructive processes involving the different joints. The intracutaneous injection of 0.3 cc. of coccidioidal toxin (coccidioidin-A) elicited only a mild local reaction (probably an anergic phenomenon).

Treatment and Progress.—Treatment with colloidal copper and coccidioidin was instituted promptly after the diagnosis of coccidioidal granuloma was established. The patient failed rapidly, however, developing signs and symptoms of cerebrospinal and other visceral involvements; she finally died on Sept. 29, 1928.

Case 7.—R. W., colored, aged 23, married and the mother of a living and healthy child, 1 year of age, came to the outpatient department of the Los Angeles General Hospital for treatment the latter part of March, 1928.

The patient said that she had always lived in Los Angeles and that she had never been to the San Joaquin valley and that, except for an attack of influenza three years prior to the present illness, she had not had any serious illness. Her present condition commenced about sixteen months before admission, with a small swelling on the lower third of the left forearm which gradually increased in size, finally ruptured and began to discharge pus. Several different physicians attempted to cure the condition by surgical and medical means; in spite of all their efforts, it persisted and progressed. She had lately begun to suffer extreme pain in the left arm, shoulder and supraclavicular region.

Examination revealed a fairly well nourished young colored woman who presented at the junction of the middle and lower third of the flexor aspect of the left forearm, a deeply infiltrated, gummatous area, about 3 cm. in size and dusky red, the center of which was covered by a closely adherent thick crust; the removal

of the crust exposed a sluggish ulceration exuding a liquid, tenacious, yellowish-gray pus. There was also marked adenopathy of the left axilla, and a gummatous mass, the size of a small orange, in the left supraclavicular area. Examination of the pus from the forearm revealed *Coccidioides immitis* culturally and microscopically.

Treatment.—Treatment of this patient was begun on April 2, and on April 6, an intradermal injection of 0.3 cc. of exotoxin (coccidioidin-A) was administered. This resulted in a characteristic reaction at the site of injection. She was then put on treatment with colloidal copper and coccidioidin-B and responded most favorably. The lesion on the forearm healed completely. The supraclavicular mass was reduced almost 75 per cent.

There was a marked increase in weight, and the patient's general condition greatly improved. Her last visit to my office was on August 13. Since that last visit she has refused to take further treatment. In reply to a letter requesting her to call at my office, she stated that she could not spare the time and that she felt perfectly well.

CASE 8.—L. I., a Mexican laborer, aged 23, entered the Los Angeles General Hospital on a stretcher, the latter part of April, 1929, and left the hospital on May 2, of his own volition and against my advice.

His reason for coming to the hospital was extreme weakness and numerous swellings and draining sinuses on different parts of the body, associated with night sweats, cough, fever and loss of weight. His present trouble had its inception about four months prior to his coming to the hospital. He was born in Los Angeles and lived there continuously until October, 1928, when he went to Fresno, Calif., where he resided until February, 1929; he was then compelled to return to Los Angeles because of illness.

Examination revealed an extremely emaciated young man who was obviously ill and in discomfort. There were numerous fluctuating and elastic tumor masses of various size involving different parts of the body and causing a good deal of discomfort and pain over the larger joints. Several of these lesions were draining freely, while the majority were unopened; the overlying skin was normal in color without any evidence of inflammatory reaction. The rise in temperature was not marked, but the pulse rate was markedly accelerated.

Roentgen study revealed destructive involvement of a number of joints and bones in different parts of the body, plus a suggestive involvement of the lungs consistent with the usual observations in coccidioidal granuloma. Examination of the pus obtained from one of the abscesses by aspiration resulted in the finding of *Coccidioides immitis* culturally and microscopically. Two injections of colloidal copper and one injection of coccidioidin-B did not make much of an impression on the condition; the patient left the hospital on April 2, at the request of his family and contrary to my advice. I have been informed that he has died.

CASE 9.—T. S., a Filipino laborer, aged 24, was admitted to the Los Angeles General Hospital on July 10, 1928, and was dismissed on July 17 because of his refusal to cooperate and to submit to proper diagnostic tests.

His complaint on admission was weakness, loss of weight, swelling and soreness of the left side of the neck, and swelling and pain of the left forearm. These symptoms had their inception six months before coming to the hospital, with a swelling of the left forearm near the elbow; then the left supraclavicular region became similarly involved.

Physical examination revealed a lump, the size of a small walnut, on the left side of the neck in the supraclavicular region; it was fixed to the overlying skin

and was dusky red. On the extensor surface, in the upper third of the left forearm, on the ulnar side, there was a firm, indurated, somewhat elevated gummatous area that was dusky red and slightly tender and painful. There was marked adenopathy of the left axilla.

Roentgen studies disclosed a destructive process of the clavicle at the acromial extremity and of the ulnar bone posteriorly just below the olecranon process, with some marginal periosteal proliferation. The patient's refusal of the suggested biopsy for purposes of tissue study resulted in his discharge from the hospital without a diagnosis of his case.

He then appeared for readmittance to the hospital, on Jan. 9, 1929. Examination at this time revealed that the original lesions were broken down and contained draining sinuses. Roentgen study of the clavicle and ulnar at this time revealed an extension of the destructive processes since the previous pictures were taken. Treatment with colloidal copper and coccidioidin-B was instituted and resulted in definite general improvement and a closing of the supraclavicular draining sinuses. However, because of constitutional and local reactions to the infections, he refused to submit to further treatment and was discharged from the hospital in April, 1929.

Case 10.—A. U., a Mexican infant, aged 3 months, was brought to the Los Angeles General Hospital on Jan. 2, 1929, with a diagnosis of pneumonia and tuberculous cervical lymph nodes. Death occurred several hours after arriving at the hospital.

The present trouble commenced twenty-one days before admission, with fever and vomiting, followed by respiratory symptoms and a flattening or sinking in of the sternal region. The patient weighed 8 pounds (3.6 Kg.) at birth, and developed snuffles and lobar pneumonia five days after birth; the condition lasted for two weeks and was followed by normal health until the present illness.

Examination at the hospital revealed an infant with marked inspiratory dyspnea who gasped at times for breath, with a temperature of 104, a pulse rate of 140, and 70 respirations per minute. At the right anterior border of the sternocleidomastoid muscle, and extending from the angle of the jaw downward about 6 cm., there was a soft fluctuating mass. The sternal and substernal regions appeared to be sunken in. Other thoracic and systemic conditions present were those commonly noted in similar respiratory and constitutional diseases and need not be dwelt on here.

Autopsy revealed the swelling at the right side of the neck to consist of an abscess which extended posteriorly from the trachea to the opposite side of the neck, though there was no clinical evidence of such an extension ante mortem. The pus in the abscess was mucinous, thick, tenacious and greenish yellow. Examination revealed the presence of *Coccidioides immitis.*

Case 11.—P. B., aged 36, an American, who had been a dairyman in the Salinas valley, California, for the previous five years, came under my care on March 9, 1929, through the courtesy of Dr. B. Frees who, after diagnosing his condition as coccidioidal granuloma, referred him to me for treatment.

His present illness had its onset in the early part of January, 1929, with fever, profuse perspiration, weakness and respiratory symptoms, for the treatment of which he was removed to the Salinas hospital where his condition was diagnosed as "double pneumonia." About four or five days following the onset of his illness, he noticed a "lump" on his chin which continued to grow in size until February 13, when his physician diagnosed it as a carbuncle and treated it by means of an incision and "extraction of the core." His pulmonary condition had

improved sufficiently after ten days' stay at the hospital to enable him to return home, but after remaining at home for a few days he was again compelled to return to the hospital because of an exacerbation of his original condition. About the middle of February, he was brought to Los Angeles to consult Dr. Frees because the local physicians had failed to establish a diagnosis; after a thorough study of the case by Dr. Frees, a diagnosis of coccidioidal granuloma was established.

My first questioning of the patient elicited the complaint of extreme weakness, profuse perspiration, extreme constipation, soreness and gas in the abdomen and marked loss of weight. Examination revealed a tall, emaciated man who was obviously ill and uncomfortable. There was a marked pyorrhea alveolaris and dental caries, and a heavily coated tongue. The chest and abdominal cavities presented evidence of a marked pathologic condition. There was a generalized adenopathy of a marked degree, and the whole abdominal wall had a boardlike rigidity. On the left side of the chin, immediately below the mucocutaneous junction there was a fungating tumor mass, the size of a large olive, which had an ulcerated, papillomatous surface and apparently involved most of the subcutaneous tissues of that area. Cautery resection of the tumor mass, and sectioning and microscopic study of the tissues revealed *Coccidioides immitis*. The intracutaneous allergic test produced a strongly positive reaction.

Treatment with colloidal copper and coccidioidin-B resulted in great improvement at first. Soon, however, a relapse set in, and the patient began to show signs of meningeal involvement. In the early part of April, he was removed to the Los Angeles Hospital with definite clinical evidence of a meningeal involvement and a spinal fluid cell count of over 300. More energetic treatment with colloidal copper and coccidioidin-B resulted finally in the subsidence of all symptoms. On April 26, he left the hospital, of his own volition and contrary to my instructions, in an apparently good condition and free from all symptoms. A few days thereafter, however, I was again requested to see him at his home because of a relapse; at that time, I requested him to return to the hospital. He persistently refused to do so. My last visit to see him was on May 9, at which time he felt somewhat improved but would not cooperate.

Case 12.—N. G., a Mexican, aged 43, was brought to the Los Angeles General Hospital in an acutely ill and semicomatose condition on April 9, 1929; he died three days after entering the hospital.

His illness had its inception four months prior to admission to the hospital; the only other data pertaining to his illness that it was possible to obtain was that his condition had been diagnosed by two physicians as meningitis.

Examination revealed an emaciated man who was critically ill, unresponsive and apparently in great discomfort. At the left nasolabial fold there was a fungating, ulcerated nodule, 1.5 cm. in size, and in the region of the sacrum were decubitus ulcers. The neck was rigid, and the pupils were unequal in size. The muscles of the extremities were atrophic and the knees much enlarged; the left knee had a draining sinus. The spinal fluid was under markedly increased pressure and slightly cloudy, but *Coccidioides immitis* was not found culturally or microscopically. Biopsy on the nasal lesion and microscopic study of its tissue disclosed *Coccidioides immitis*.

Roentgen examination revealed a destructive process in the right patella, left knee and left tibia. In view of the extreme condition of the patient, no treatment with copper was given, and he died on April 12.

Autopsy.—Autopsy disclosed considerable emaciation. Both knees were considerably swollen, with some evidence of fluid; over the left patella there was a draining sinus in the skin, from which a large amount of chocolate-colored, creamy fluid exuded on pressure. There was considerable crepitation of the left patella. There was a fungating nodule, 1.5 cm. in diameter, at the left nasolabial fold. The left pupil was considerably larger than the right. Moderate decubitus ulcers were found over the sacrum. Around the brain stem and in the sylvian fissures there was a moderate number of soft "tubercles," on the average a trifle larger than a pinhead, and involving only the pia. No purulent meningitis and no lesions in the brain or cerebellum proper were shown. The ventricles were normal. The middle ears, the cavernous sinus and the sphenoidal sinus were normal. The pleural cavities contained no free fluid. There were slight adhesions on the right side. Externally, the lungs appeared normal, but both bases showed moderate areas of firmness; throughout the lungs, miliary shotty nodules could be palpated, although they were not noticable at first. On section, the apexes showed normal air-containing lung tissue. There were, however, numerous miliary, glistening hyaline dots similar to small miliary tubercles; these were scattered uniformly throughout the rest of the lung, with congestion or early consolidation in the bases. The bronchial lymph nodes were small and blackish. The heart and the pericardial cavity were normal. The abdominal cavity and all the abdominal viscera were essentially normal. The spleen was normal in size. Section showed only questionable white, tubercle-like dots. The terminal ileum and cecum were normal. The testicles were small and normal. When the left knee was incised, the medial one fourth of the patella was found to be eroded and necrotic, and the tibia in a large area about the tubercle was eroded. The joint surfaces of the femur were not involved, but the joint surface of the tibia was involved. The right knee showed involvement of the capsule of the joint and also of the joint surface of the tibia, but there was much less destruction of bone here. The cause of death was given as coccidioidal granuloma, involving the nose, lungs and knees.

Case 13.—A. D., a Filipino, aged 27, an elevator operator, entered the Los Angeles General Hospital on Jan. 3, 1929, and died there on February 1.

His illness began two months before, with cough, fever, weakness, night sweats and loss of weight. These symptoms continued to grow worse, and a month before admission he had a hemorrhage from the stomach.

Examination by the intern in the tuberculosis service revealed an emaciated young man, who weighed 118 pounds (53 Kg.) and was obviously critically ill Examination of the chest revealed a generalized involvement of both lungs; examination of the sputum, on January 10, revealed tubercle bacilli. On the nose and right cheek there were several grayish-red, firm nodules, which were neither tender nor painful. Roentgen study of the chest revealed a condition of the lung that suggested tuberculosis. The condition of the patient continued to grow worse. Because of the skin lesions on the face, a member of the dermatologic staff was called in consultation and suggested a biopsy on one of the lesions. This biopsy was performed on January 26, and resulted in the finding of *Coccidioides immitis* on January 30, a few hours before the patient died.

ABSTRACT OF DISCUSSION

Dr. Morrow, San Francisco: Dr. Jacobson is to be complimented on bringing this subject before the section. His photomicrographs are the best I have seen, and deserve special mention. Dr. Cummins of San Francisco also presented

a paper on coccidioidal granuloma in one of the other sections, and I think was awarded a medal in the scientific exhibit. About 200 cases have been reported in the last few years, most of them from California. Evidently, many patients have died from *Coccidioides immitis* infection without the diagnosis having been made. This applies particularly to the cerebral cases, the mediastinal cases, and to a less extent, the visceral cases. The cutaneous type is the one of most interest. The lesions are found as nodular pustules, as sinuses, and as cutaneous and subcutaneous abscesses. If a drop of pus is taken from a subcutaneous nodule or from a pustule or abscess, I think it is easy to make the diagnosis. These double-capsulated bodies are easily seen with a 1/6 lens. The treatment must be carried out accordingly.

Most of the cases in California occur in persons who come from the lower San Joaquin Valley, and because this part of the valley is nearest to Los Angeles, the physicians there see the greatest number of them. Dr. Jacobson has been fortunate in that his patients were in the group of subacute cases. Most of the cases we have seen have been malignant, and the patients have died within from a few weeks to a few months. It is the subacute case which gives some hope for cure. Dr. Jacobson has been fortunate in getting fairly good results from the copper preparations. During the last few months, Dr. Carl Meyer of the University of California has been preparing a vaccine for the patients whom we have had to treat. He has been working on a vaccine in which the double-contoured bodies are in great preponderance. Apparently we get better results from this than we do from the vaccines made from the mycelia.

DR. TEMPLETON, Oakland, Calif.: Recently Dr. Chipman and I reported a case of a young Mexican who had never been in the San Joaquin Valley but had worked in one of the cotton mills that received its supply of cotton from the San Joaquin Valley. About six months after starting to work in this mill, he noticed a swelling of the lymph nodes in the left cervical region; shortly after this an abscess appeared over the left scapula. At that time he received diagnoses of carcinoma, syphilis and Hodgkin's disease. Skin lesions appeared about a year later on the right side of the neck, and shortly afterward on one of the fingers of the right hand and on the left hip. Still later, destructive lesions appeared in these areas and over the scapula. The patient received tartar emetic combined with roentgenotherapy locally, colloidal copper intravenously and iodides by mouth and intravenously. He did not improve, however, under any of these treatments. He failed rapidly, and on May 1, 1929, he was in the hospital in a desperate condition. At that time he presented a condition which I have never seen mentioned anywhere—mycotic plaques on the pharynx which contained *Coccidioides immitis*. He had no pulmonary involvement. About that time I talked with Dr. Jacobson. We injected a copper preparation intramuscularly, with the vaccine that Dr. Morrow mentioned, and the patient responded markedly. He had been in a critical condition. The sinuses had all been discharging and he could not eat because of the mycotic plaques on the pharynx. Today he is apparently well and wants to return to work. We do not know, unfortunately, whether the copper compound or the vaccine was responsible for the recovery, but certainly in this one case colloidal copper, given intramuscularly, plus the vaccine produced startling results.

DR. CUMMINS, San Francisco: I have listened with much interest to the paper and discussion. As Dr. Morrow said, with Dr. Smith and Dr. Halliday I presented a small contribution to the Section on Medicine at this convention. We reviewed 182 cases of coccidioidal granuloma and were assisted by the Cali-

fornia State Department of Health in the preparation of the material. We found that Mexicans contribute the largest percentage of cases, 31 per cent. The race which contributed the highest mortality was the negro, 63 per cent. There was a total mortality of 68 per cent in the series. We realize that Dr. Jacobson sees a little more localized cases than we do, and the mortality is perhaps higher in the cases that we see. We consider it a grave disorder which must not be confused with tuberculosis and blastomycosis, particularly with tuberculosis. For diagnostic purposes it is most important that sufficient laboratory examinations be made, such as examinations of the pus and biopsy specimens, as Dr. Jacobson said. With guinea-pig inoculation, these examinations are most important.

In regard to treatment, we are convinced that, if a patient has an early, distal lesion only, there is one line of treatment that will be probably efficacious, and that is liberal amputation of the part. As a result, our first patient (Southern Pacific Hospital) is alive today. We are uncertain as to the best drug to use. We have tried a number of preparations, including colloidal copper. Our feeling is that tartar emetic must be considered. At our scientific exhibit, a case of supposed laboratory infection was reported as having been cured by the alternating administrations of tartar emetic and roentgen rays. We emphasize the fact that the disease has a high mortality and that it closely simulates tuberculosis.

DR. SCHOLTZ, Los Angeles: We in Los Angeles see more than our share of cases of coccidioidal granuloma, and we usually refer our cases to Dr. Jacobson for further study.

Clinically, diagnosis is usually made by the exclusion of other types of infectious granulomas. The most striking clinical feature of coccidioidis is its tendency to attack deep structures, such as the lungs, bones, joints, etc. It seems that skin lesions, usually of gummatous type, are the least common point of entry. In most of the cases, at least, the invasion of deep structures can be demonstrated in the presence of coccidioidal lesions of the skin. Copper colloid apparently gave better therapeutic results than older remedies. In one case, however, in which injections of a copper compound had to be discontinued because of systemic reactions, the intravenous use of gold sodium thiosulphate and diathermy locally gave unexpectedly definite symptomatic improvement, both local and systemic. It appears that the therapeutic and serologic method introduced by Dr. Jacobson offers a distinct advance in the clinical control of this dreaded malady.

DR. JACOBSON: I appreciate the generous attention which the discussers have accorded this paper. I am especially grateful to Dr. Morrow for his complimentary comments on the quality of the slides and for his other thoughtful remarks on the classification of the cutaneous lesions, types of the disease, etc. I regret exceedingly not to be able to confirm Dr. Scholtz's observations on the effect of injections of a gold compound in this disease. It so happens that the patient whom he referred to as having responded favorably to this type of therapy belongs to my series of cases and was, of course, the subject of my observation while he was under Dr. Scholtz's care, after being discharged from my service for refusing to cooperate or to receive injections of a copper compound and coccidioidin. I noticed no evidence of improvement in his condition as a result of injections of a gold compound.

I cannot subscribe to the pessimistic views of Dr. Cummins in connection with the treatment. I believe that when the local lesions of this disease are confined to the terminal portion of an extremity, an effective treatment is the application of carbon dioxide without pressure through a layer of paraffin for from five to

eight hours, or radical excision with the actual cautery combined with injections of a copper compound and coccidioidin. High amputations of the involved extremity because of an isolated lesion on its terminal portion, as advocated by Dr. Cummins, is somewhat analogous to the Chinese method of curing corns by chopping off the toes. As to the usefulness of tartar emetic in the treatment of this disease, all that I can say is that it has been tried at the Los Angeles General Hospital extensively without visible results. Dr. Emil Beck informs me that while radium has no effect on the ameba in the test tube, in the presence of the heavy metals the effect is profound and lethal. (This may account for the favorable results obtained by Dr. Guy in his case.) I shall utilize this information in connection with colloidal copper.

Dr. Templeton's point about the patient not responding to the intravenous injections of a copper compound but showing rapid improvement following intramuscular injections is worthy of greater emphasis. It definitely coincides with my experience.

CUTANEOUS MELANOMA

A HISTOLOGIC STUDY ESPECIALLY DIRECTED TOWARD THE STUDY OF MELANOBLASTS *

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Pigmented malignant neoplasms are among the most serious tumors afflicting mankind. They are fortunately rare, which fact has militated against a clearer conception of their origin and nature. Ewing [1] stated: "The peculiar and obscure conditions of its origin, the remarkable physiologic properties of the chromatophores (melanoblasts—author) in the animal kingdom, the eccentricities of its clinical course and its interesting history as a field of debate render this tumor one of the most notable topics in oncology." Many authors have written on this subject, more recently Dawson [2] and Miescher.[3] Difficulties in interpretation on solely morphologic grounds have been partially overcome by the functional approach to the problem of melanin pigmentation, which phase of biologic activity lends itself well to study, since it furnishes a visible end-point.

NORMAL PIGMENTATION

Consideration of the pigment problem may be found in recent publications.[4] The salient features may be briefly summarized. Cutaneous pigment is formed by specialized cells (melanoblasts) present in the basal layer of the epidermis, in the hair matrix and deep in the corium in mongolian spots, blue nevi and in certain animals, such as the ape. Melanin is present normally in these cells in round or oval granules,

* Submitted for publication, Oct. 11, 1929.

* From the Division of Dermatology of the Department of Medicine of the University of Chicago.

* Read before the Section on Dermatology and Syphilology at the Eightieth Annual Session of the American Medical Association, Portland, Ore., July 12, 1929.

* The publication of this work has been aided by a grant from the Douglas Smith Foundation for Medical Research at the University of Chicago.

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all of the same size. Phagocytic cells in the papillae and superficial dermis, which are not capable of forming pigment but obtain it elsewhere, are known as "chromatophores." Their pigment is in granules of irregular size and shape, and tends to be somewhat lighter in color than in melanoblasts. Epidermal melanoblasts are often branched, and are then known as dendritic cells. Considerable confusion has been occasioned by terminology. Melanoblasts are often called chromatophores, and dendritic cells are often called Langerhans' cells, with which they have nothing in common except shape. Much of the error has resulted from the tendency to call all melanin-containing cells having processes or branches "chromatophores." Biologic study has shown that melanoblasts and chromatophores are different types of cells. A little experience enables one to differentiate them in normal human skin, but in some animals and in melanotic tumors it is often impossible without special methods.

CHEMISTRY OF MELANIN

Melanin is evidently formed by the action of an intracellular ferment (oxydase) on a melanogen. Bloch demonstrated a reaction between 3, 4-dioxyphenylalanin, called "dopa" for convenience, and an oxidizing factor in the pigment-forming cells (melanoblasts), producing a black melanin-like substance. The most important feature of this reaction is a diffuse blackening of the entire cellular protoplasm, which tends to appear granular in faint reactions. The leukocytes are also blackened, due to the polyphenolase which they contain. The reacting factor in the melanoblasts behaves as a ferment, and has been called "dopa-oxydase." The exact nature of the melanogen has not been determined. Raper [5] discovered that tyrosinase acting on tyrosine produced first dioxyphenylalanin, then 5, 6-dioxyindol and later 5, 6-dioxyindol-2 carboxylic acid (fig. 1).

ORIGIN AND NATURE OF MELANOBLASTS

The origin of melanoblasts has not yet been satisfactorily explained. It is believed by many that they are of both ectodermal and mesodermal origin, the ectodermal cells being the palisade basal cells and dendritic epidermal cells, and the mesodermal, the mongolian cells and those of the blue nevus. The epidermal dendritic cells are assumed to be altered basal cells, and therefore of ectodermal origin. Smith [6] made cultures of

5. Raper, H. S.: Tyrosinase-Tyrosine Reaction; Production of *l*-3 4-Dihydroxyphenylalanine from Tyrosine, Biochem. J. **20**:735, 1926; Tyrosinase-Tyrosine Reaction; Production from Tyrosine of 5:6 Dihydroxyindole and 5:6 Dihydroxyindole-2-Carboxylic Acid, Precursors of Melanin, ibid. **21**:89, 1927.

6. Smith, D. T.: The Pigment Epithelium of the Embryo Chick's Eye Studied in Vitro and in Vivo, Bull. Johns Hopkins Hosp. **31**:239, 1920; Evidence Showing Existence of Two Different Types of Pigment Cells Capable of Giving Rise to Melanotic Tumors, ibid. **36**:185, 1925.

embryonal retinal and choroidal pigment cells. The former propagated in a solid sheet, resembling epithelium, and the latter individually as do fibroblasts. He observed the formation of pigment granules in these cells (rods and grains respectively). He assumed by analogy that the skin also contains two types of melanoblasts, one epithelial and

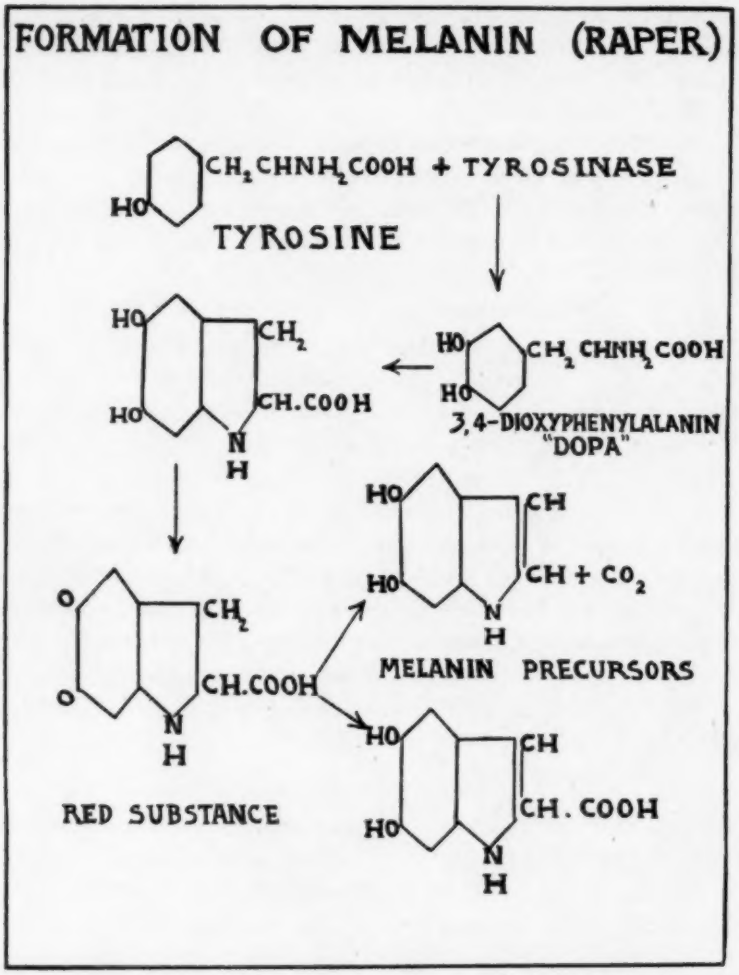

Fig. 1.—Diagrammatic presentation of substances resulting from the action of tyrosinase on tyrosine. Note that the first substance is dioxyphenylalanin "dopa," which is used in the dopa reaction.

the other dermal, but made no mention of epidermal dendritic cells. Other authors[7] assumed a common origin of epidermal and dermal melanoblasts, and stated that epidermal melanoblasts have wandered into

7. Masson, P.: Les naevi pigmentaires, tumeurs nerveuse, Ann. d'anat. path. **3**:417 and 657, 1926.

the epidermis, and supply pigment to the basal cells through the melanoblastic dendrites.

At any rate, it is certain that not all basal cells actively form pigment at the same time. The dopa reaction is normally intermittent and appears continuous only in thick sections of tissue involved in marked pigment activity. The dopa reaction is demonstrated in frozen sections, often from 20 to 30 microns thick, which causes the dopa positive cells to appear more numerous than they would appear in thin paraffin sections.

The differentiation of two types of cells in the basal epidermis presents several difficulties. Dendritic cells filled with pigment can be easily identified if they course in the plane of the section. Study of the dendritic type of cell shows that they differ morphologically from the palisade basal cells. The latter have finger-like processes projecting into the dermis. The long axes of their nuclei are at right angles to the surface. Pigment is apt to be massed at the distal pole of the nucleus. The dendritic cells, on the contrary, may have their long axes in any direction (fig. 9); the pigment is distributed throughout the cell, and often appears more dense along the surface. The author has attempted to identify dendritic cells after their pigment has been completely bleached by means of chlorine dioxide, and has been unable to do so. Some of the cells at the epidermodermal junction may be said to be of the dendritic cell type because of their smooth dermal surface, long axis of nuclei parallel to the cutaneous surface and the appearance of vacuolation, which is found at times in dendritic cells. The dopa reaction lends support to the theory of two types of cells. The author has examined thousands of sections of skin showing this reaction and has never seen a typical columnar basal cell showing a positive dopa reaction. The dopa positive cell never presents a dentate border toward the dermis, and the cells often show actual or rudimentary branching (fig. 8). Bloch and others believe that the dendritic cell is merely a modified basal cell, possibly changed by functional activity. Transitional forms have never been convincingly demonstrated.

Masson [7] and other authors expressed the belief that the melanoblast originates from some part of the peripheral nervous system. He maintained that melanoblasts furnish pigment through their branches directly to the palisade basal cells. This is difficult to determine in normal adult skin, but several facts support this hypothesis. The first demonstrable sign of pigment function is the positive dopa reaction in dendritic embryonal cells. This is followed by pigment granules in these cells, and later by pigment granules in adjacent columnar cells. Pigmented dendritic cells are more prominent in the skin of infants in comparison to basal cell pigmentation than in adults. The slighter degree of

pigmentation, of course, makes their identification easier. In oral and pharyngeal mucosa, where pigment may be almost exclusively in dendritic cells, the only other pigment granules discernible are scattered in other cells about the terminal portions of the dendrites. In contrast to this, Bloch called attention to a type of melano-epithelioma (pigmented benign epithelial growth) showing marked pigmentation with considerable capping of pigment at the distal pole of the nuclei, in which no dendritic cells could be discovered. It is not impossible, however, that such cells may have been present at an earlier stage, since the author has found them in this type of tumor, to be mentioned later.

Early hyperpigmentary processes are characterized by the presence of dendritic cells, and later the palisade basal cells contain much pigment. In acanthotic processes the palisade cells contain little pigment, and dendritic cells are often prominent.

BENIGN MELANOTIC NEOPLASMS

Study of pigmented neoplasms is even more fascinating than study of normal pigmentary processes. Benign lesions include pigmented nevi, blue nevi, melano-epithelioma (little known type of benign tumor recently discussed by Bloch [8]) and the so-called lentigo maligna. Malignant lesions have been designated both melanocarcinoma (nevocarcinoma) and melanosarcoma, depending on their supposed origin and individual cell morphology. Owing to the fact that a single tumor may exhibit cells with epithelial and fibroblastic configuration, conservative pathologists designate all pigmented tumors as "melanoma." Tumor cells seem always to originate from melanoblasts, hence "melanoblastoma," a term somewhat used, would be scientifically more correct. Brevity and usage make the term "melanoma" preferable, qualified by "benign" or "malignant" as desired.

Two types of pigmented benign epithelioma are exemplified by Bloch's cases: [8]

The first case presented a group of about eight lesions arranged concentrically on the lateral thoracic wall. Each lesion was from 0.5 to 1 cm. in diameter, and elevated from 4 to 5 mm. above the surface. They were an intense bluish brown and were covered by a delicate thin crust. Histologically, a majority of the cells were of the basal cell type, with islands of prickle cells scattered throughout. Some of these contained horny pearls, with no stratum granulosum intervening. The third type of cell was the dendritic cell, scattered throughout.

The tumor in the second case was a solitary, slightly papillary nodule, dark brown, slowly growing and clinically similar to malignant

8. Bloch, B.: Ueber benigne, nicht naevoide Melanoepitheliome der Haut nebst Bemerkungen ueber das Wesen und die Genese der Dendrittenzellen, Arch. f. Dermat. u. Syph. **153**:20, 1927.

melanoma. Histologically, the tumor was seen to be epithelial, multiloculated, with many deep invaginations filled with keratinized masses. Mitotic figures were rare. The cells showed much basal type of pigmentation with much capping. The dendritic type of cell was not found. Case 1 illustrates a tumor of this type.

CASE 1.—A man, aged 59, presented a lesion in the left groin which had started two years previously as a small "wart." It had become gradually larger and a dark line developed downward from the lesion. The lesion itself had been insensitive, and no sensory changes had been noted. The lesion was a small tumor, 1 by 2 cm., pedunculated (fig. 2), pointing upward and outward and elevated about 1 cm. It was dark brown and had keratotic plugs, which could not be expressed. Extending downward from the inferior extremity of the tumor was a slightly elevated lesion of the same color, 0.5 by 1 cm.

Histologic section revealed the growth to be largely epithelial, with an insignificant connective tissue pedicle (fig. 3). The epithelial surface was invaginated, and contained masses of cornified epithelial cells. The stratum corneum was

Fig. 2 (case 1).—Tumor removed from the groin.

thickened in these places. The stratum granulosum was normal. The stratum germinativum was markedly thickened, the cells were smaller than in acanthotic processes, such as condyloma acuminatum, and the nuclei were hyperchromatic. Sections treated with silver nitrate showed marked pigmentation in the palisade basal cells, and also a moderate number of dendritic melanoblasts at the epidermodermal junction. The papillae were narrow and long. No nevus cells could be found. Chromatophores were present in the papillae and pedicle. A diagnosis of pigmented epithelioma was made.

PIGMENTED NEVI

Pigmented nevi present two factors for consideration: first the nevus cells, and secondly, alteration of normal pigment activity. The nevus cell question per se is not so important in a consideration of malignant melanoma, since the neoplasms probably do not arise in nevus cell nests, but always from melanoblasts at the epidermodermal junction, or from dermal melanoblasts of the blue nevus. The formation of the nevus cell is of interest, however, as it is also a melanoblastic cell and may represent a form of benign proliferation thereof. Old theories

of the origin of nevus cells from endothelium and chromatophores have been abandoned. They are now considered to be melanoblastic cells similar to those found at the epidermodermal junction. Various conceptions have arisen from the examination of many static sections, which

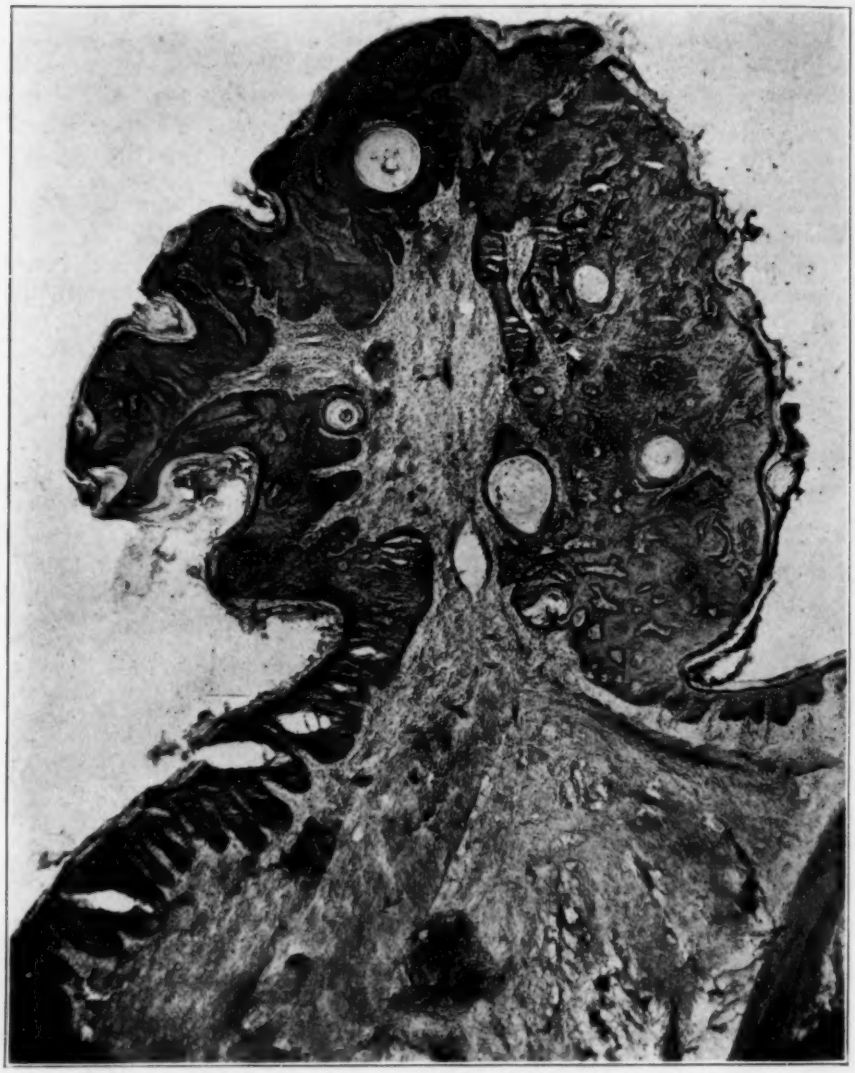

Fig. 3 (case 1).—The growth is produced mainly by epithelial proliferation. Hematoxylin and eosin; low power.

are at best merely theories. The first theory, first championed by Unna, and accepted by perhaps a majority of dermatologists today, assumes alteration of basal cells, with descent into the dermis. The second, originally advanced by Soldan and recently revamped by Masson,[7]

assumes two types of cells in the basal epidermis. The first is the palisade basal cell and the second is the melanoblast. The melanoblasts and nevus cells are assumed to have a common origin, and Masson expressed the opinion that they originate from the sheath of Schwann.

The important and heretofore largely neglected feature of pigmented nevi is the pigment activity of the epidermis. It is only the modern study of pigment that has made this possible. The lesions show increased numbers of melanoblastic cells. They may be confined to the epidermodermal junction, and appear attached to the epidermis. The following case illustrates a lesion in which all melanoblasts were attached to the epidermis.

Case 2.—A girl, aged 26, presented a smooth, dark brown lesion, 4 by 10 cm., on the shin (fig. 4). It had been present since birth and had enlarged with her growth.

Figure 4

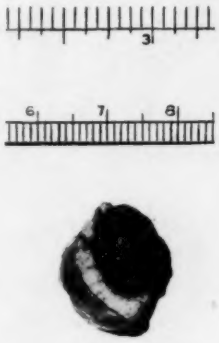

Figure 5

Fig. 4 (case 2).—About one fourth of the lesion, a smooth brown nevus located on the shin.

Fig. 5 (case 3).—Pedunculated pigmented nevus.

Microscopic section showed only changes in the epidermis. The surface was slightly hyperkeratotic and presented several invaginations containing keratinized epithelium. The rete processes were elongated and clubbed. Marked hyperpigmentation was evident throughout the basal and adjacent layers, especially at the tips of the rete processes where the pigment was often dense enough to obscure cytologic structure. The epidermis adjacent to the lesion was normally pigmented. The superficial dermis contained many chromatophores. No nevus cells were found.

Under oil immersion lens an increased number of melanoblasts was evident throughout the section. They were for the most part limited to the epidermodermal junction (fig. 10). The proximal surface of the cells was smooth. Distally, from one to several branches often extended into or along the epidermis. Pigment granules, round or ovoid, filled the cells more or less completely. The same type of granules was found in the basal cells, with much capping. A moderate number of pigment granules could be seen extending into the stratum cor-

neum. In places the melanoblasts were arranged in syncytial masses, but were always attached to the epidermis. Many chromatophores were seen in the papillae and superficial dermis.

The process may be interpreted as hyperpigmentary due to an increased number of melanoblasts at the epidermodermal junction. None of them is separated from the epidermis, as in the fleshy mole, where one sees the so-called nevus cells in masses or cords in varying numbers, generally detached from the epidermis. In these cell masses, only the more superficial cells contain pigment. The melanoblastic cells in con-

Fig. 6 (case 3).—High power view of the positive reacting cells in the basal layer and in the superficial nevus cell masses. Dopa reaction.

tact or just beneath the epidermis show a marked dopa reaction. The following case illustrates such a lesion.

CASE 3.—A soft, dark brown lesion, 1 by 1 cm. (fig. 5), was removed from the back of a woman, aged 36. In sections treated with silver nitrate, the epidermis was thinned but not disintegrated. Pigmentation was largely in basal cells, with a few melanoblasts attached to the epidermis. Melanin granules were seen in all cells, even to the surface. The superficial nevus cells were smooth, oval and pigmented. Chromatophores were present in the superficial dermis. The dopa reaction (fig. 6) showed positive cells intermittently in the basal layer of the epidermis, presenting a smooth surface proximally and a few branches distally, extending into the epidermis. Some of the smooth, ovoid superficial nevus cells also reacted. No reaction was seen in the chromatophores.

The melanoblastic epidermal cells of a nevus may be dendritic (fig. 7).

Pigmentation of the epidermal cells may be of the early type (stippled with pigment granules) or of the late type (capping of pigment granules distal to the nucleus). One may find all gradations in various nevi, even in the same lesion.

If the lesion has shown signs of clinical progression, one finds a zone of increased pigment activity about the border, with many dendritic cells.

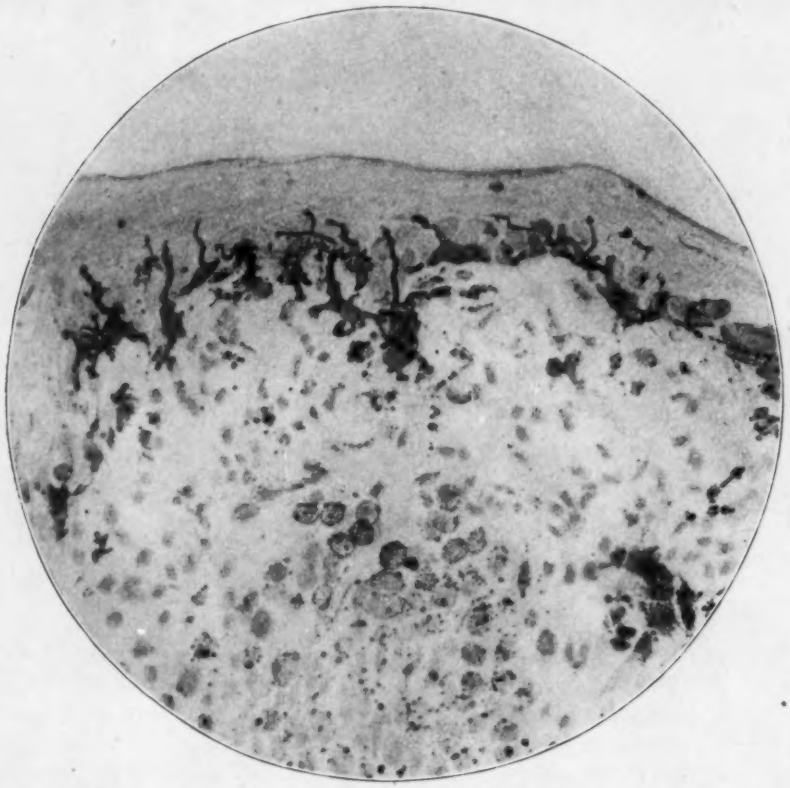

Fig. 7.—Soft brown nevus. There are dendritic melanoblasts at the epidermodermal junction. Oval and round pigmented nevus cells are seen in the dermis. Oil immersion; silver nitrate reaction, pyronin methyl-green stain.

In the light of the importance of pigment activity, it may be seen that the degree of hyperpigmentation does not govern the severity. Bloch [9] stated that from the standpoint of possible malignancy, the most dangerous lesion is the soft brown nevus. The idea that the black or the bluish-black lesion is dangerous may have arisen from the fact that such lesions are malignant, and may have already metastasized.

9. Bloch, B.: Personal communication to author

BLUE NEVUS

As stated previously, deeply lying melanoblasts produce a bluish discoloration. This is exemplified in the mongolian spot, a bluish lesion found in the sacral region. Bahraway [10] found melanoblasts in the sacral region of all children examined up to the age of 12 years. I examined the skin of the sacral region of eight American born infants up to 2 weeks of age and found such cells in only one instance. This is too small a series from which to draw definite conclusions, but it is evident that they are not found in every child. The blue skin of the ape is

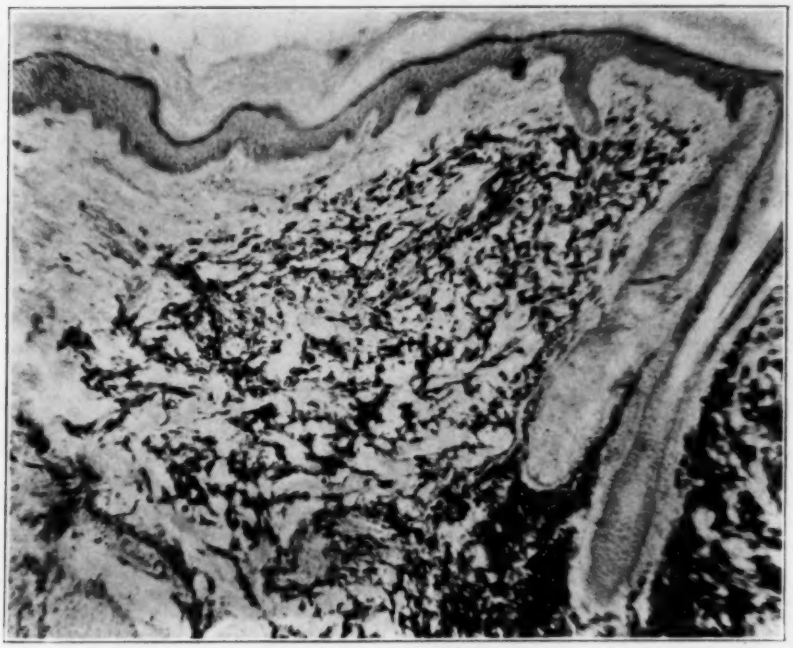

Fig. 14 (case 4).—Low power view. The epidermis is only slightly pigmented. In the dermis there are numerous pigment-containing melanoblasts, grouped especially about the glands and vessels. These are the cells found in the ape's skin and mongolian spots. The deeply lying pigment produces a blue coloration. Hematoxylin and eosin.

due to the presence of melanoblasts deep in the corium. The following case is one of blue nevus.

CASE 4.—A nurse, aged 30, presented a blue macule on the forearm just below the elbow. She said that she had not noted the lesion longer than six months. It was excised. The section was 1 cm. in length. In the center, extending for 0.5 cm., was a brownish discoloration. The epidermis was slightly elevated in this region.

10. Bahraway, A. A.: Ueber den Mongolfleck bei Europäern, ein Beitrag zur Pigmentlehre, Arch. f. Dermat. u. Syph. **141**:171, 1922.

Microscopically, the epidermis was slightly thickened over the lesion, and showed moderate pigmentation. Immediately beneath the epidermis, the dermis contained only a few chromatophores. Beneath this, it was diffusely pigmented in a sharply circumscribed region (fig. 14). The pigment was brown, and tended to be massed about the follicles, gland ducts and vessels. Where not too dense, the pigment was seen to be contained in elongated cells, coursing parallel to the collagen bundles. The cells often had more than one terminal process. The pigment granules were yellowish brown, ovoid and uniform as regards size and shape. These cells were the same type of melanoblasts as those found in the ape's skin and in mongolian spots.

LENTIGO MALIGNA

Lentigo maligna is a macular, markedly hyperpigmented lesion, generally found in old people. Miescher [3] found that 75 per cent of his malignant melanomas arose from lentigo maligna and only 25 per cent from pigmented nevi. The following case is illustrative of this type of lesion.

CASE 5.—A markedly hyperpigmented lesion was present on the temporal region of an old man. It was excised. On histologic examination, the stratum corneum was loose, slightly hyperkeratotic and retained in epithelial invaginations. The stratum granulosum was normal. The stratum germinativum was thin over the papillae, but the rete processes were thickened and clubbed. The basal and adjacent layers were markedly pigmented. The superficial dermis contained many chromatophores.

In silver preparations (fig. 15) under very high power, the marked pigmentation was seen to be limited to the basal and immediately adjacent cells. Pigment granules could be seen, however, to extend into the stratum corneum. The basal cells were mostly of the columnar type. Pigment granules were diffusely distributed, but some capping was evident in places. In the more markedly pigmented regions, a few dendrites could be seen extending between the palisade basal cells. Rarely could they be seen connected to cells. The dopa reaction was positive intermittently in the basal layer. Branches were only occasionally visible.

This process may be interpreted as marked pigmentation, with some localized activity at the present time.

MALIGNANT MELANOMA

Transition from benign to malignant melanoma is gradual. The following case illustrates such transition.

CASE 6.—A woman, aged 30, presented a smooth, slightly elevated light brown lesion, 0.8 cm. in diameter. She said that the lesion had been present since birth, but had been enlarging for four months. It was excised.

The stratum corneum was hyperkeratotic. The stratum granulosum was intermittent. The dermis was involved in slight round cell infiltration, largely perivascular. A few nevus cells were grouped in some of the papillae and in the superficial dermis. The collagen fibers of many of the papillae were hyaline. Although the change from the periphery to the center of the lesion was gradual, the section could be roughly divided into three parts (fig. 16).

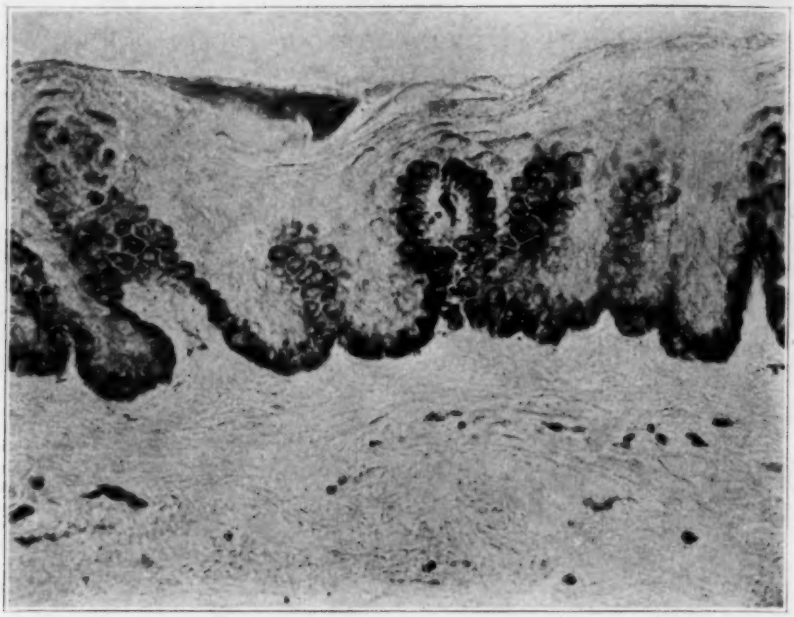

Fig. 15 (case 5).—Lentigo maligna; low power view. The basal portion of the epidermis is markedly pigmented and rete processes are clubbed. Very few melanoblasts can be identified. Silver nitrate reaction, pyronin methyl-green stain.

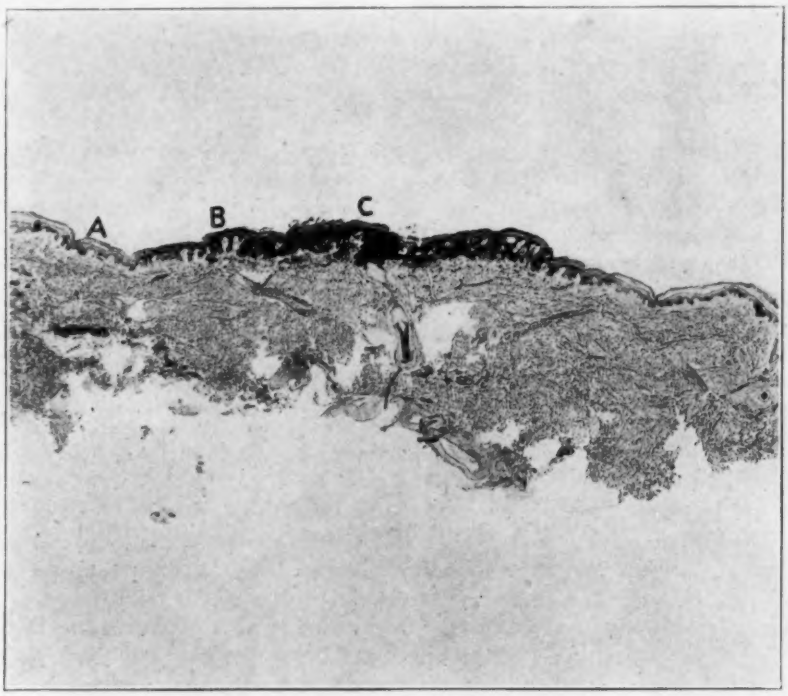

Fig. 16 (case 6).—Borderline melanoma; very low power, for orientation. Region *A* represents the location of figure 11; *B*, figure 12, and *C*, figure 13. Silver nitrate reaction, pyronin methyl-green stain.

At the periphery (fig. 11), beyond the clinically hyperpigmented border, many dendritic cells could be seen at the epidermodermal junction, sending branches into the epidermis. Pigment was present in the cells in the form of uniformly sized oval granules. The palisade basal and adjacent cells contained granules of the same type, diffusely distributed, with no capping distally to the nucleus. This portion may be said to be involved in hyperpigmentary activity, without much hyperpigmentation.

Toward the center of the lesion (fig. 12) the dendritic cells increased in numbers, and were less uniform in their arrangement. They were seen in the superficial dermis in variously shaped masses, with considerable vacuolation. Dendrites were not definite. The palisade basal cells were fairly uniform and markedly pigmented, with much capping distal to the nucleus. Pigment granules, both in melanoblasts and in basal cells, were in larger masses, irregular in size. The same large masses could be seen extending to the surface in smaller amount.

In the center of the lesion (fig. 13) the epidermis was disintegrated and markedly pigmented, even to the surface. Melanoblasts were present in greater numbers, with no definite arrangement, in masses containing many vacuoles. The cells were mostly elongated, with nuclei of various sizes and shapes. No mitotic figures were seen, and only a few cells appeared to contain more than one nucleus. They extended in masses into the superficial dermis, rather sharply limited. Beneath these masses were many chromatophores. The epidermal cells also had no definite arrangement, and appeared torn apart, with much vacuolation. Narrow cords of these cells extended deeply and were lost in the masses of melanoblastic cells. Concentrically arranged cell masses were seen some distance from the surface, with stratum granulosum and keratinized cells. These were evidently the horny pearls of Miescher and Gans. Tracing them through serial sections showed that they were merely invaginations of the surface epithelium, and in no way comparable to the horny pearls of the squamous cell carcinoma. Pigment granules were in masses of irregular size and shape both in the melanoblasts and in the epidermal cells, even to the surface.

Considering the entire lesion in its various aspects as different stages of one and the same process, it may be stated that the initial process is one of increased pigment activity without hyperpigmentation, then increase in number and disintegration of the melanoblastic cell masses with hyperpigmentation of the epidermal cells, and finally disintegration of the epidermal cell structure and penetration of the melanoblasts into the deeper dermis.

When the process has definitely become malignant, the melanoblastic cells penetrate into the dermis and are also cast off with the stratum corneum. Figures 17 and 18 illustrate a malignant melanoma which was removed from the sole of the foot. Histologically, there was sudden transition from normal to pathologic tissue. The stratum corneum was thinned and contained isolated and grouped melanoma cells. The stratum germinativum was disintegrated and extended deeply in long strands. Between these strands and among the epidermal cells were masses of tumor cells, most of them containing melanin. The tumor mass and the superficial dermis contained a few chromatophores. A few

Fig. 17.—Low power view of malignant melanoma of the sole of the foot (see fig. 18). Malignant cells are extending deeply and also are being cast off in the stratum corneum. Hematoxylin and eosin.

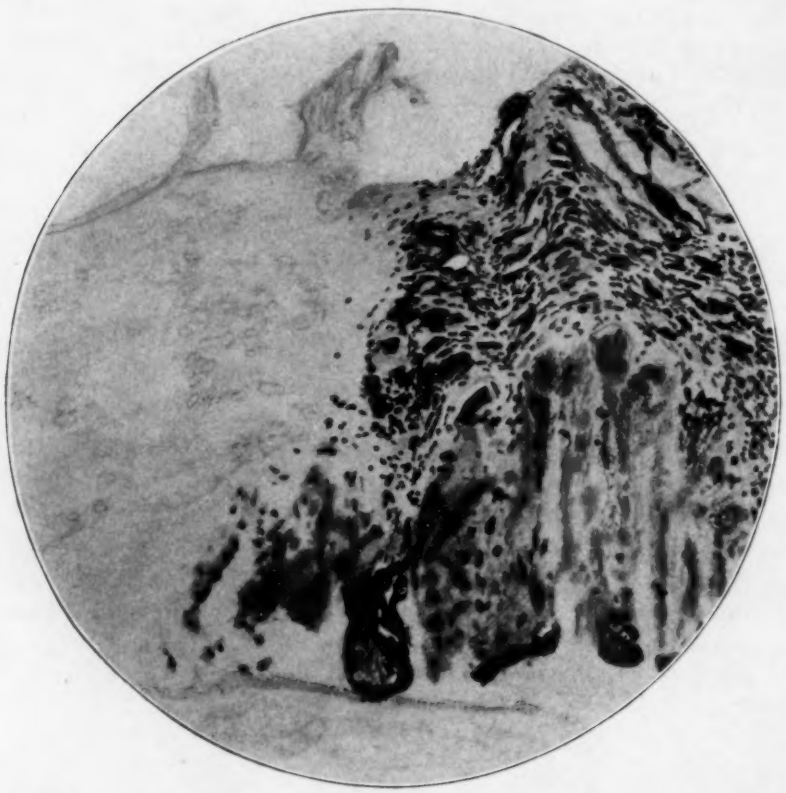

Fig. 18.—Low power view of a malignant melanoma from the sole (see fig. 17). The malignant cells show the reaction throughout, even as they are being cast off in the stratum corneum. Dopa reaction.

lymphocytes were seen just beneath the tumor mass. Under high power practically no mitotic figures could be seen and very few multinucleated cells. The dopa reaction was intense in the tumor cells, even in those within the stratum corneum.

Malignant melanoma tends to metastasize early to the lymph glands. This is thought to be due to the lack of cohesion between the cells, such as is present in epidermal carcinoma.

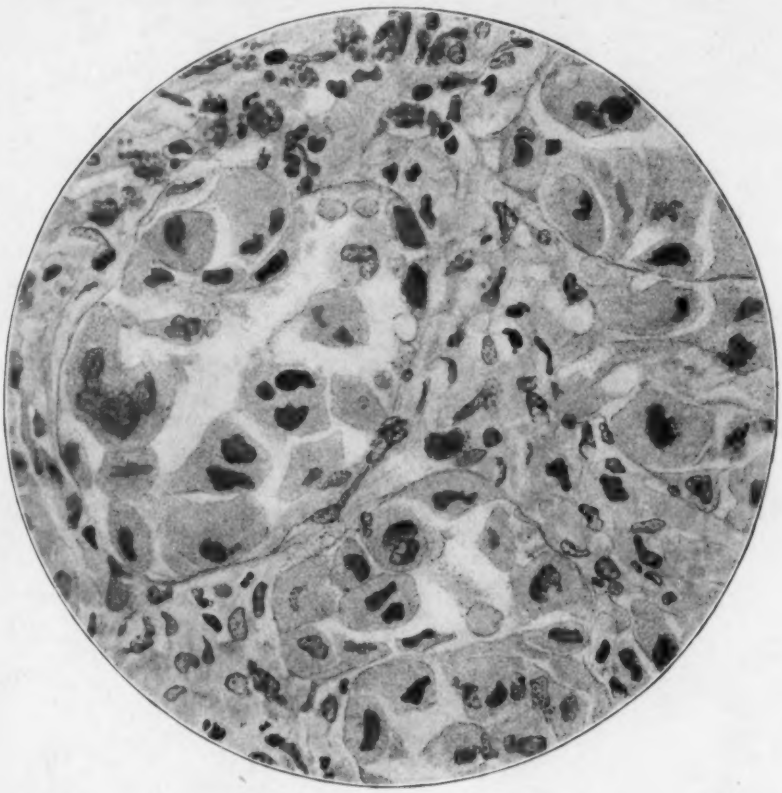

Fig. 19 (case 7).—Metastatic melanoma of the lymph gland of the axilla. Polynucleated cells, some containing melanin are seen. There are chromatophores in the upper portion. There are no mitotic figures. (The glands had been treated by the roentgen ray one month before death). Oil-immersion; hematoxylin and eosin.

Case 7 (Courtesy Dr. Gideon Wells).—A mole, reported to have been but one-eighth inch (0.3 cm.) in diameter, was removed from the left arm of a woman, aged 26, in July, 1928. Histologic examination had not been made. In November, roentgen treatment had been given to the enlarged glands in the left axilla. She died in December from acute endocarditis, complicated by pregnancy of five months' duration.

Autopsy revealed a metastatic nodule in the wall of the heart, and enlarged axillary glands. The glandular growth (fig. 19) was composed of cells varying from large multinucleated giant cells to the predominating cells, which were of medium size, but had abundant cytoplasm. In places a pseudo-alveolar arrangement was present. Areas of necrosis and scar tissue were present, the latter containing numerous chromatophores. An occasional tumor cell was seen to contain a slight amount of pigment. A diagnosis of malignant melanoma was made.

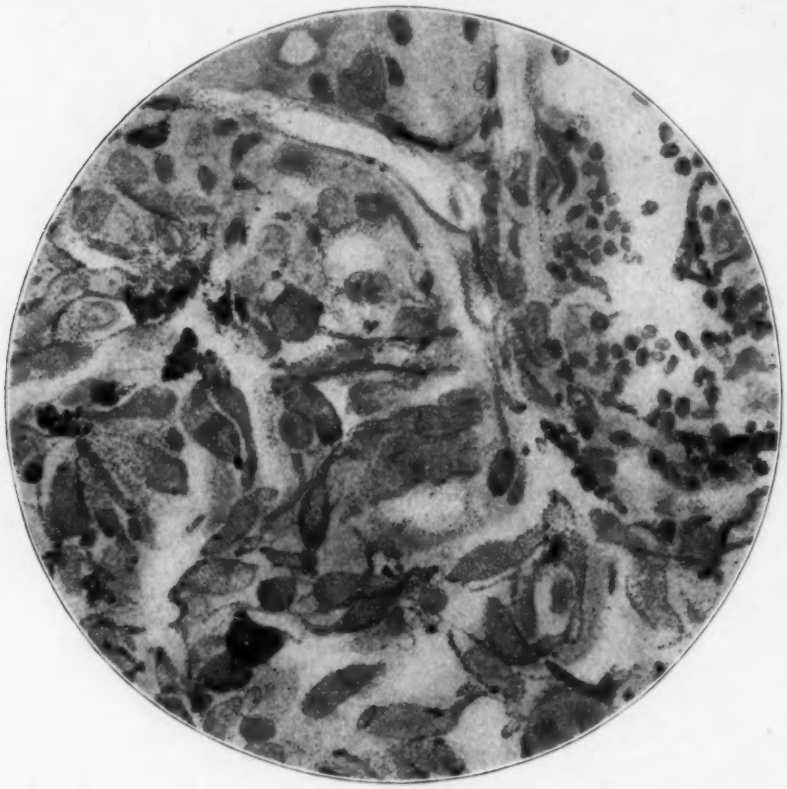

Fig. 20.—Metastatic melanoma of the lymph gland. The cells are predominantly dendritic. No mitotic figures can be seen. Oil-immersion; silver nitrate reaction, pyronin methyl-green stain.

In contrast to this picture is the following metastatic glandular lesion. The gland was infiltrated by masses of large cells (fig. 20). Some of them were oval or round, similar to nevus cells, while others were elongated. Perhaps a majority of the cells were pigmented, and most of the pigmented cells were elongated with one process at each end. Pigment was present in the form of small granules of uniform size distributed throughout the cell. The pigmented cells showed no evidence of nuclear division, but the nonpigmented ovoid cells showed a moderate number of what appeared to be mitotic figures. No multinucleated cells were seen in the pigmented portions.

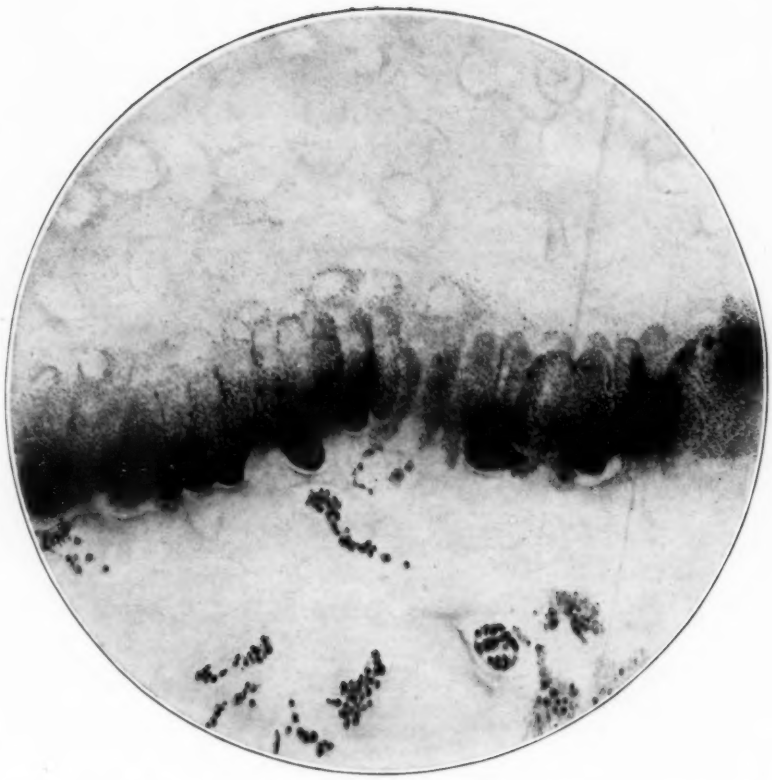

Fig. 8.—Prepuce. Melanoblasts are identified by the positive reaction, and are situated at the epidermodermal junction. Palisade basal cells can be identified by finger-like projections into the dermis. Oil-immersion; dopa reaction.

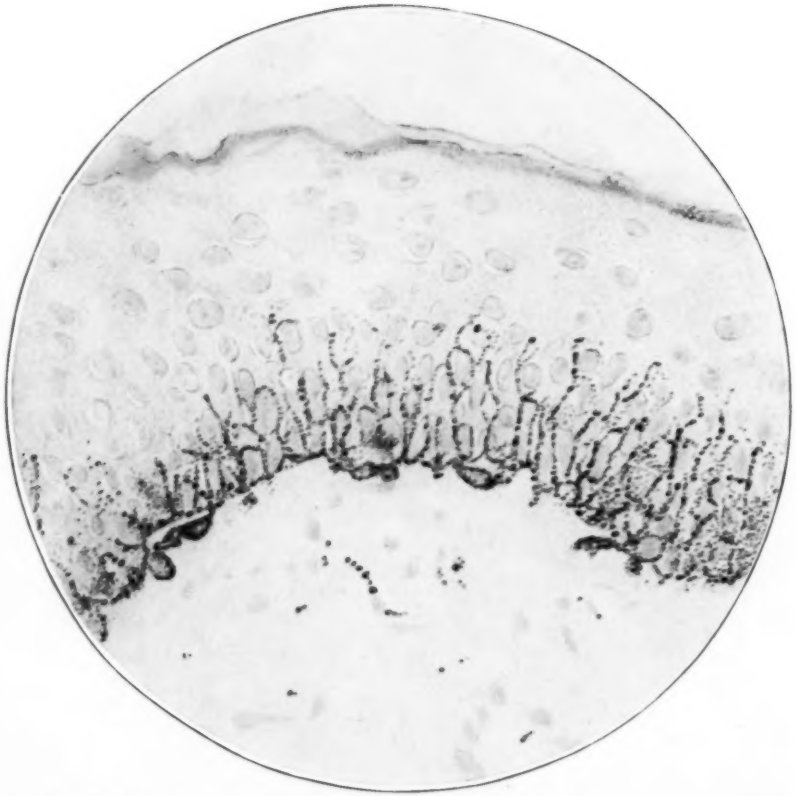

Fig. 9.—Nipple of a woman, aged 77, who died from bronchopneumonia, following severe burns. The pigmentation is slight, mostly in the dendritic melanoblasts at the epidermodermal junction. These cells have been neglected in textbooks on histology. Silver nitrate reaction, pyronin methyl-green stain.

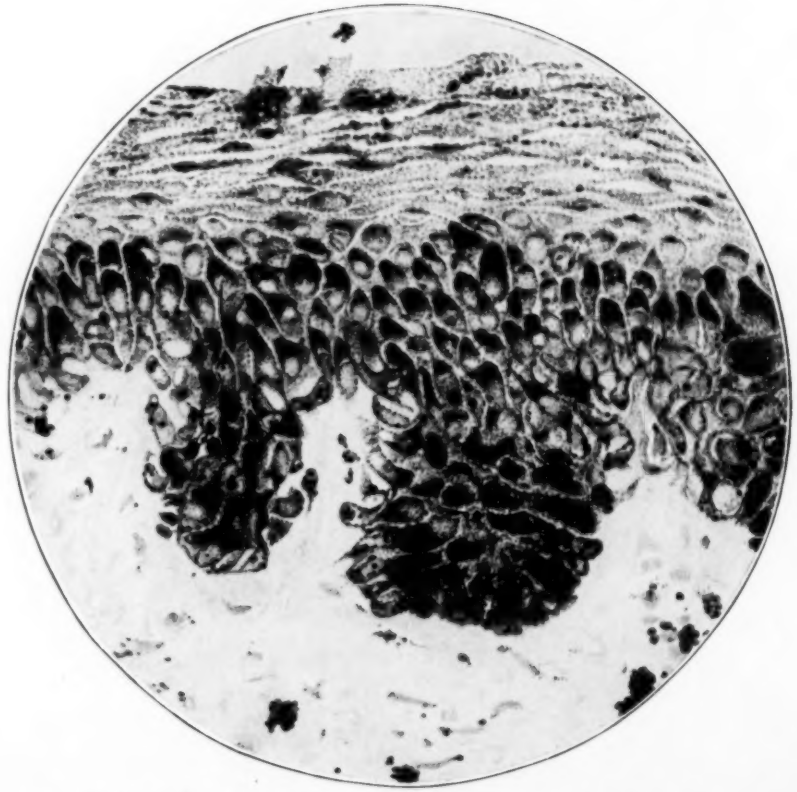

Fig. 10 (case 2).—Marked pigmentation in the palisade cells, with much capping of the pigment above the nuclei. There is a marked increase in the number of melanoblasts at the epidermodermal junction. Oil-immersion; silver nitrate reaction, pyronin methyl-green stain.

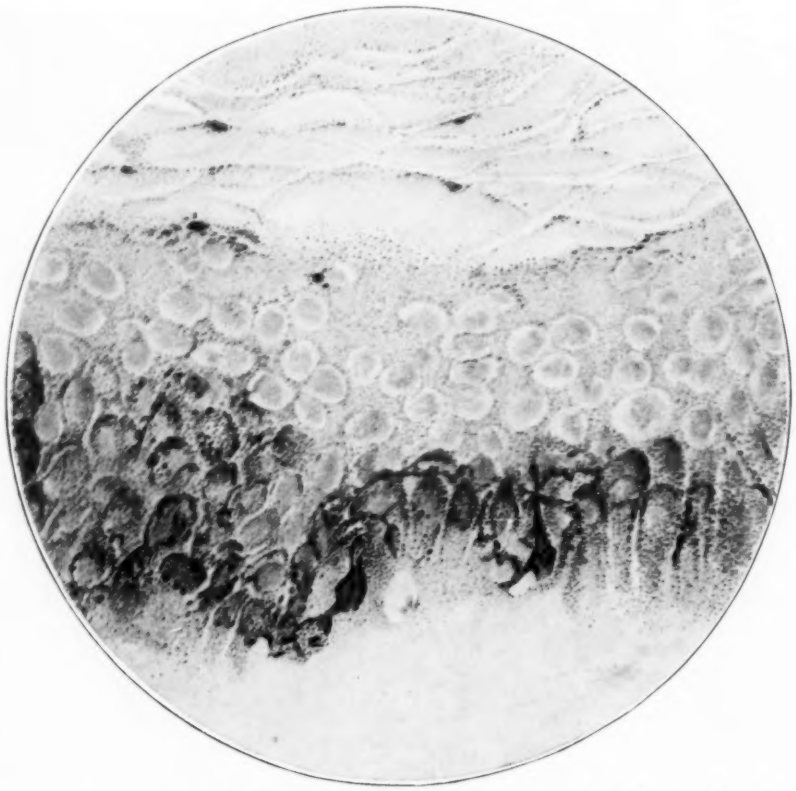

Fig. 11 (case 6).—Borderline melanoma; region of *A*, figure 16. Dendritic melanoblasts are prominent. There is a slight pigmentation in the palisade basal cells. Oil-immersion; silver nitrate reaction, pyronin methyl-green stain.

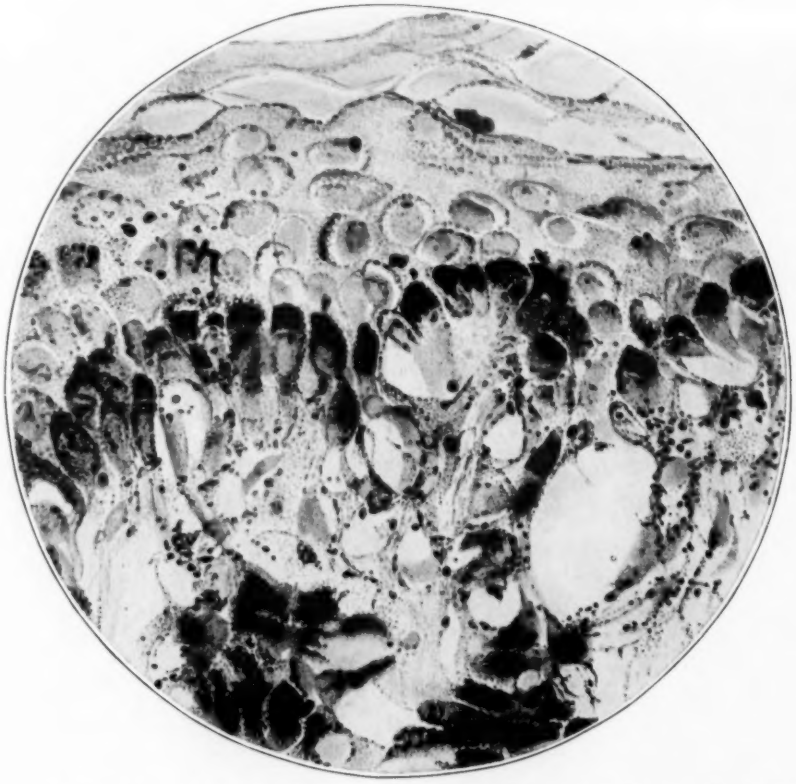

Fig. 12 (case 6).—Borderline melanoma, region of *B*, figure 16. The melanoblasts are increased in number, with much vacuolation. The palisade basal cells are markedly pigmented, with capping of the pigment above the nucleus. Oil-immersion; silver nitrate reaction, pyronin methyl-green stain.

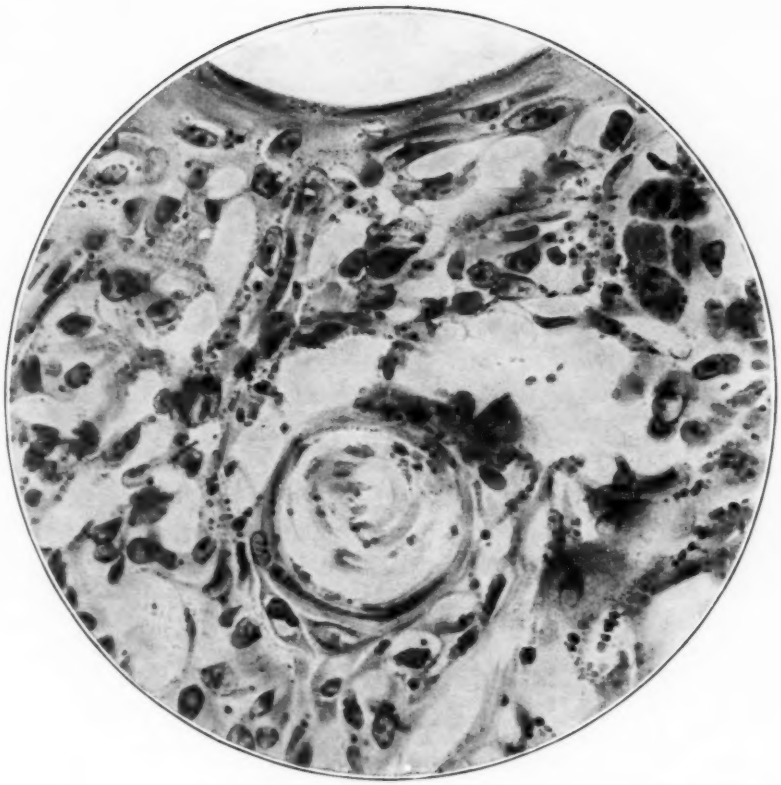

Fig. 13 (case 6).—Center of a borderline melanoma, region of *C*, figure 16. The epithelial cells are disorganized. The "horny pearl" is merely invagination of the surface epithelium. Oil-immersion; hematoxylin and eosin.

CONCLUSIONS

Normal pigmented skin contains melanoblastic cells located at the epidermodermal junction, differing in morphology and function from the palisade basal cells. They are found in larger numbers in smooth pigmented nevi and fleshy moles. They evidently are the cells constituting malignant melanoma.

The morphology and functional characteristics of these cells favor the idea that they are not derived from the palisade basal cells, but are an independent cell type. Those with much branching are similar to cells found in the central nervous system, and they may have a nerve origin.

In one specimen of enlarging borderline melanoma, the periphery showed increased pigment activity; within this was a hyperpigmentary process found in many nevi, and in the center both the epidermal and the melanoblastic layers were disorganized, similar to the condition found in malignant melanoma.

Metastatic lesions contain cells similar to the melanoblastic cells, but never similar to the pigmented palisade basal cells.

Melanoma seems to be benign or malignant proliferation of melanoblasts normally found in all pigmented epidermis.

ABSTRACT OF DISCUSSION

DR. FINNERUD, Chicago: Dr. Becker's excellent paper and his display in the Section Exhibit have been most interesting to me. The determination of the degree of pigment activity is of great scientific and, of course, some practical importance. In this particular work, Dr. Becker has correlated satisfactorily the early malignant lesions with what is known regarding normal pigmentation. In the light of our present knowledge, it seems that the classification and nomenclature employed by him probably would be good for us to follow. It is important that a uniform system be adopted, in that in the past there has been so much confusion regarding simple matters. For example, as one reviews the literature, one often finds that there is confusion between the terms "melanoblast" and "chromatophore," whether or not the author is referring to the pigment-forming cells.

I should like to ask Dr. Becker his reason for including melano-epithelioma with benign neoplasms. I presume he means by this only Bloch's basal cell epithelioma with pigment.

Although several phases of the pigment problem still remain unsolved, progress has been made in the last few years, principally by Bloch and his associates, and we hope that the investigation and progress will continue.

DR. BECKER, Chicago: By the term melano-epithelioma, I refer to the nonnevoid pigmented benign epithelioma recently discussed by Bloch, and not true melanoma. This term has been applied to true melanoma, but the usual term is melanocarcinoma, nevocarcinoma or melanosarcoma. The preferable term seems to be melanoma, qualified by benign or malignant.

COMPARATIVE STUDY OF THE KAHN AND HINTON REACTIONS *

NATHAN NAGLE, A.B.
AND
JOSEPH C. WILLETT, D.V.M.
ST. LOUIS

An opportunity was afforded to compare the test for syphilis recently proposed by Hinton with the Kahn reaction, which is the standard method in these laboratories. The technic of the two tests was carried out strictly in accordance with the directions of the respective authors.[1] Dr. Hinton furnished the antigen for his test. Table 1 summarizes the results given by the two methods with 748 serums. Of this number, 363 were positive with the Kahn test and 299 were positive with the Hinton test. Sixty-nine serums were positive with the Kahn and negative with the Hinton test, and five were positive with the Hinton and negative with the Kahn test.

An attempt was made to determine the clinical histories of the seventy-four cases which showed divergent results. Data were obtained on only forty-four of these cases, which are presented in table 2. It is evident from this table that the Kahn reaction was positive and the Hinton negative in thirty-eight cases of syphilis, while the Hinton test was positive and the Kahn negative in two cases of syphilis. In cases in which the patients were presumably free from syphilis, three + reactions were obtained with the Kahn test and one ++++ reaction with the Hinton test. A + reaction is significant only in the presence of a positive history and clinical evidence of syphilis; however, for the purpose of this study such reactions are included with the positive reactions.

We experienced some difficulties with the Hinton test which must be overcome before the test becomes practical. Dr. Hinton stated in regard to the end-results of his test that, ". . . clearing with no agglutination indicates that the temperature has been too high, or the incubation period too long, or both." [2] We found it necessary to

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* Submitted for publication, Oct. 16, 1929.

* From the St. Louis Health Division Laboratories.

1. Hinton, W. A.: Boston M. & S. J. **196**:993, 1927; J. Lab. & Clin. Med. **14**:621, 1929. Kahn, R. L.: The Kahn Test, A Practical Guide, Baltimore, Williams & Wilkins Company, 1928.

2. On one occasion all of the Hinton tests were positive after the usual incubation period. As several serums from this group came from nonsyphilitic cases and were negative with the Kahn test, we were unable to account for the apparent false positives and therefore excluded them from the study.

discard the results of eighty tests because at the end of the sixteen hour incubation period all showed a distinct clearing. Several of these serums were obtained from known cases of syphilis and were positive with the Kahn test. The temperature was correct at the time the tests were

TABLE 1.—*Comparison of Kahn and Hinton Reactions Based on 748 Examinations*

Number of Cases	Kahn Reaction	Hinton Reaction
206	++++	++++
12	++++	+++
13	++++	++
19	++++	—
11	+++	++++
7	+++	+++
14	+++	++
2	+++	+
12	+++	—
3	++	++
3	++	++++
5	++	+++
6	++	—
7	+	++
9	+	+
2	+	±
32	+	—
1	—	++++
1	—	+++
2	—	++
1	—	+
380	—	—
Total 748	363 positive 385 negative	299 positive 449 negative

TABLE 2.—*Clinical Histories of Cases Showing Divergent Serologic Reactions*

Number of Cases	Kahn Reaction	Hinton Reaction	Clinical History
1	++++	—	Syphilis, treated, Kahn quantitative 40 units
2	++++	—	Tertiary, no treatment
2	++++	—	Secondary, no treatment
6	++++	—	Tertiary, treated
1	++++	—	Secondary, treated
3	+++	—	Tertiary, treated
3	+++	—	Syphilis
2	++	—	Tertiary, no treatment
4	+	—	Tertiary, treated 2 years
1	+	—	Primary, positive dark field, lesion 3 weeks' duration, no treatment
3	+	—	No history of syphilis
2	+	—	Syphilis, treated, previous Wassermann ++++
1	+	—	Latent, treated, previous Kahn ++++
1	+	—	Secondary, treated
2	+	—	Syphilis, no treatment
1	+	—	Neurosyphilis, treated 2 months
3	+	—	Tertiary, no treatment
3	+	—	Primary, no treatment
1	—	+++	Tertiary, treated 3 years; primary lesion 15 years ago
1	—	+	Tertiary, treated 2 years
1	—	++++	No clinical signs or history of syphilis
Total 44	41 positive 3 negative	3 positive 41 negative	

placed in the incubator and when they were removed. If the clearing in all tests is to be attributed to a higher temperature than 37 C., we can explain this occurrence only by assuming that the temperature in our incubator went up during the night and adjusted itself during the morning.

SUMMARY

Of 748 comparative tests made with the Kahn and Hinton methods, 363 serums were positive with the Kahn reaction and 299 were positive with the Hinton reaction. The clinical histories secured in forty-four of the seventy-four cases giving divergent serologic reactions showed the Kahn test resulting in thirty-eight positive reactions in syphilitic cases with negative Hinton reactions, and the Hinton test resulting in two positive reactions with negative Kahn reactions. The Kahn test gave three + reactions and the Hinton test one + + + + reaction in cases not diagnosed clinically as syphilis. In our experience, the Hinton test is not comparable to the Kahn test in sensitiveness and practicability.

LICHEN SPINULOSUS

FOLLOWING INTRADERMAL APPLICATION OF DIPHTHERIA TOXIN *

S. WILLIAM BECKER, M.D.
CHICAGO

Lichen spinulosus represents a type of follicular reaction. The individual lesion presents grossly a flat to conical, slightly inflammatory or noninflammatory element 1 mm. in diameter, bearing a hairlike, horny spine (spinulus) often containing a lanugo hair. Removal of the parakeratotic spine reveals a tiny funnel-like orifice. The lesions appear simultaneously or in crops, and involve more commonly the nape of the neck, buttocks, trochanteric regions, flexor surfaces of the knees, extensor and flexor surfaces of the arms and the abdomen. The face, hands and feet are usually spared.

Microscopic examination shows the process to be limited to the follicle. In the early stages, the vessels are slightly congested, and slight effusion may be noted. The follicle usually exhibits marked atrophy; the epithelium is parakeratotic, as is the lamellated corneous plug.

The acute type may be a form of trichophytid (lichen trichophyticus), a form of arsphenamine dermatitis,[1] or due to an unknown cause. More chronic are spinulous lichen scrofulosorum and the spinulous type of follicular syphilid and lichen ruber planus. The most chronic type is the more or less permanent variety, appearing in crops, and remaining permanently.[2] The spinulous elements may occur as part of another dermatosis. The author has recently seen this type of follicular reaction in toxic dermatitis following the administration of gold sodium thiosulphate and in perifollicular seborrheic dermatitis of long standing.

Intradermal application of diphtheria toxin in the performance of the Schick test seems to be the causal factor in the following case:

A boy, aged 6, was given intracutaneous diphtheria toxin. At the usual time, about forty-eight hours later, a strongly positive reaction was evident. A day or two following this, a generalized eruption appeared, consisting of erythematous

* Submitted for publication, Jan. 17, 1930.

* From the Division of Dermatology of the Department of Medicine of the University of Chicago.

1. Stauffer, H.: Lichen spinulosus als Salvarsanexanthem, Arch. f. Dermat. u. Syph. **154**:217, 1928.

2. Crocker, H. R.: Diseases of the Skin, Philadelphia, P. Blakiston's Son & Company, **1**:452, 1905.

follicular papules from 0.5 to 1 mm. in diameter. The lesions persisted as such for two weeks, when they faded, and at this time the spinous element was noted. The palms and soles were desquamating slightly. The spinous lesions persisted for two or three weeks, when they gradually disappeared. About five or six weeks after the Schick test the skin became normal.

Comment.—This case presents some similarities to other inflammatory cases. Bloch [3] stated that the spinulous lesions are not primary in lichen trichophyticus, but secondary to an inflammatory, partly follicular, partly eczematous exanthem, which gradually fades into the typical lichen trichophyticus. Stauffer's patient [1] first presented an eczematoid arsphenamine exanthem, later lichen spinulosus. The lesions in my case were purely follicular, markedly erythematous, and after the erythema subsided, the typical spinulous eruption appeared. The eruption was peculiar in that it was generalized, even the palms and soles being affected.

One may conclude from a study of this type of reaction that the follicular apparatus acts collectively as a unit in response to certain noxa, just as the epidermal cells in eczema, the superficial vascular system in the erythemas, in dermatitis of the scarlatiniform and exfoliative types and in urticaria. The agent directly responsible for the reaction is unknown. It may be either the involved toxin (trichophytin, diphtheria toxin, etc.) or products formed by action of these noxa on some other tissue of the body. No case similar to the one here reported could be found in the literature. The various dermatoses accompanying clinical diphtheria have recently been discussed by Glanzmann.[4]

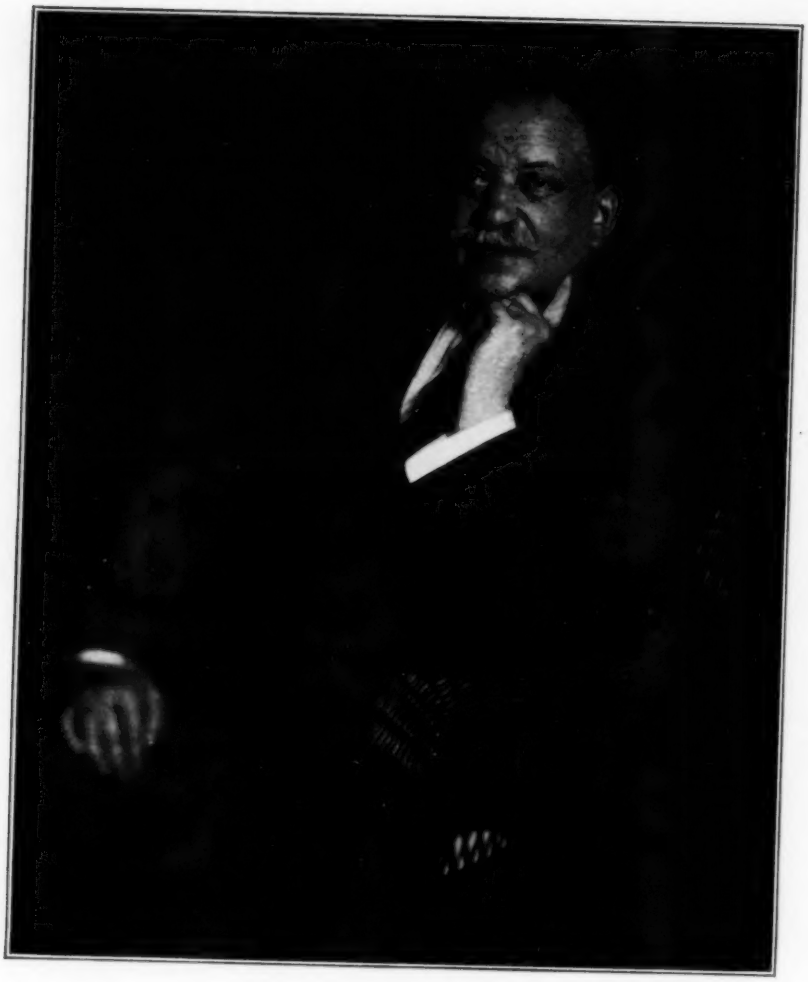
SUMMARY AND CONCLUSION

A case of lichen spinulosus following a positive Schick test is reported. The lesions were erythematous for two weeks and spinous for two or three weeks. It is possible that diphtheria toxin may be folliculotoxic in rare instances.

Lichen spinulosus represents a reaction of the follicular system to various agents, infectious agents or their toxins (*Trichophyton* and other fungi, tubercle bacilli, *Spirochaeta pallida,* the diphtheria bacillus), chemical agents, such as arsphenamine, and other agents of unknown nature. Careful search for all possible causal factors must be made in all cases.

3. Bloch, B.: Die Trichophytide, Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer **11**:564, 1928.

4. Glanzmann, E.: Ueber die Syntropie von Eiterungen, Erythema Exsudativum Multiforme, Anaphylaktoider Purpura und Diphtheria, Jahrb. f. Kinderh. **119**:1, 1928.



LUDWIG WEISS, M.D.

1852–1930

Obituary

LUDWIG WEISS, M.D.

1852-1930

Dr. Ludwig Weiss was born on Feb. 7, 1852, at Esztergom, Hungary, and died on Feb. 14, 1930, in New York. At the age of 17 he went to Vienna, and after five years of study he graduated from the university in 1877. A short time later he began the practice of medicine in New York. He was chief of the dermatological and genito-urinary department of the German Polyclinic (of which he was a charter member) since 1883, a lecturer on skin diseases at the New York Post-Graduate School and Hospital (1893-1895) and a consulting physician of the St. Mark's and Peoples hospitals. The welfare of the German Polyclinic, of which he was president for many years, was very close to his heart, and he labored with enthusiasm and untiring effort to secure its enlargement and the erection of a hospital. At the time of his death, he was recording the history of the institution for inclusion in an annual report.

Dr. Weiss became a member of the German Medical Society in 1878, the New York County Society in 1885, the New York Academy of Medicine and the American Medical Association in 1902, the Manhattan Dermatological Society in 1903 and the American Dermatological Association in 1914. Through his membership in these various societies, he was well known to most of the readers of the ARCHIVES, and was beloved by all who knew him intimately. While engaged in general practice, he devoted most of his time and attention to dermatology and urology and contributed many valuable articles in both German and English to the current medical literature. Among these may be mentioned:

The Abortive Treatment of Phlegmon by Resorcin Inoculation, Vicarious Elimination of Mercury Through the Saliva, Notes on Urethral Asepsis, Venereal Prophylaxis That Is Feasible, Pityriasis Rosea, an Erythematous Eruption of Internal Origin, Hyperidrosis Pedum and Its Treatment by Potassium Permanganate, Erythema Induratum of Bazin, The Prostitution Problem in Its Relation to Law and Medicine, Syphilis in Children, and Parakeratosis Ostracea (Scutularis).

Dr. Weiss also translated several books from German into English and from English into German. Among the latter were Marion Sim's "Story of His Life" and Roosa's "Diseases of the Ear." He was greatly

interested in Koch's tuberculin therapy, in the roentgen treatment of skin disease and in the study of endocrine glands in their relation to various dermatoses.

At a memorial service held at the Academy of Medicine on March 16, under the auspices of the Ladies Auxiliary Society of the German Polyclinic, many of his friends were gathered, and representatives of the Polyclinic (of which he was president from 1900 to 1905), the Deutsche Medicinische Gesellschaft (of which he was an honorary member), the Manhattan Dermatological Society (of which he was president in 1905) and the Mount Neboh Masonic Lodge united in paying tribute to the memory of their departed friend. Evidently all present had been deeply impressed by the unvarying geniality of his disposition and by the exceptional kindliness of his nature. In the words of Rabbi Stephen S. Wise, "He was a friend of men, a man who took his calling seriously and gave to it all that was in him—his best powers, his entire strength, his utter consecration. He was a true physician. As such he ministered to men, as such he will be remembered and his name long be blessed."

G. H. F.

Abstracts from Current Literature

Basal Metabolism in Dermatological Conditions. B. Throne, New York State J. Med. **30**:259 (March 1) 1930.

A report is made of tests on the basal metabolism in 340 patients suffering from various dermatoses. The technic used and the limits considered normal are not described. Lupus erythematosus and pemphigus showed a tendency to high readings.

Williams, New York.

Letter from Brazil. J. Darier, Ann. de dermat. et syph. **10**:1169 (Nov.) 1929.

Darier's letter contains a number of interesting notes on tropical dermatoses seen during a sojourn in Brazil. The original is not adapted to abstract but will repay reading.

Hypertrophic Hemangiectasia of Parkes-Weber. L. M. Pautrier and A. Ullmo, Ann. de dermat. et syph. **10**:1195 (Nov.) 1929.

Pautrier and Ullmo report the first French case of this disorder. They review the literature and agree that the condition is an independent entity. Their patient was 17 years of age, and the disease had been present for three years. It affected the right leg which was enlarged but not edematous. On the back of the foot and extending some distance up to the leg were variously sized lesions from light to dark brown. On palpation, dilated subcutaneous veins could be perceived.

The patches had a smooth or slightly plicated surface and were elevated. They recalled, to some degree, the aspect of old regressing patches of lichen planus.

Histologic examination exhibited a peculiar angiomatous structure. Large veins were present immediately beneath the epidermis and scattered throughout the cutis. In some areas there were glomerular vascular structures.

The authors believe that the disease is a congenital malformation. They obtained satisfactory results with cryotherapy.

Epileptiform Psychosis from Thallium Acetate. J. G. Uruena, Ann. de dermat. et syph. **10**:1210 (Nov.) 1929.

Uruena's article consists of a critique of a report of a case by Bachkevitch and Prokoptchouk (*Ann. de dermat. et syph.* **10**:383 [April] 1929) of this complication following the administration of thallium. Bachkevitch and Prokoptchouk's patient was 20 years of age and had favus. According to Uruena, thallium was contraindicated in this case. When used in adults, the maximum dose is 0.3, which is sufficient to produce epilation. Epilation with thallium will not cure favus, according to Uruena's experience in twenty-three cases.

A Fatal, Mutilating Case Showing Features of Sarcoid and Lupus Pernio. L. Chatellier, Ann. de dermat. et syph. **10**:1213 (Nov.) 1929.

Chatellier's patient was a young man without significant previous history or manifestations of tuberculosis. The disease began on the nasal mucosa and slowly and progressively invaded the skin of the cheeks, lips and mouth, destroying the tissue which it attacked. On the nose, characteristic symptoms of lupus pernio were present. Histologic examination revealed a tuberculoid structure.

The affected tissue was almost lignous in density on the margins. Fever and other systemic toxic symptoms were present. At one time, an eruption suggesting papulonecrotic tuberculid appeared. Death occurred about a year after the onset.

The report of the autopsy and some animal experimentation are not included in the article, but are to be reported later.

The author regards the case as a malignant form of lupus pernio. Both clinically and histologically there were features that showed close relations to sarcoid.

SOME RARE EXOTIC DERMATOSES. P. PHOTINOS, Ann. de dermat. et syph. **10**:1231 (Nov.) 1929.

This article contains a brief description of a number of unusual or rare diseases observed in Greece. Photographs of moulages made from the cases illustrate the text.

BASAL CELL CANCER OF THE PENIS TREATED BY SURGICAL DIATHERMY. GIACARDY and DURAND-DASTÈS, Ann. de dermat. et syph. **10**:1256 (Nov.) 1929.

The authors reported this case because of the comparative rarity of this type of cancer of the penis and the excellent result obtained by diathermy. There has been no recurrence, but the observation period was only one year.

ACRODERMATITIS CHRONICA ATROPHICANS. M. PINARD, RABUT AND C. GAUTHIER, Bull. Soc. franç. de dermat. et syph. **36**:755 (July) 1929.

Examination of this patient showed a moderate sympathicotonia and hyperthyroidism.

ACRODERMATITIS CHRONICA ATROPHICANS. PETGES, LECOULANT and MOUGNEAU, Bull. Soc. franç. de dermat. et syph. **36**:756 (July) 1929.

The authors report a typical case of acrodermatitis chronica atrophicans, the first seen in Bordeaux in twenty-three years.

SIX NEW CASES OF ACRODERMATITIS CHRONICA ATROPHICANS. L. M. PAUTRIER, P. LANZENBERG and A. ULLMO, Bull. Soc. franç. de dermat. et syph. **36**:760 (July) 1929.

Pautrier reiterates his belief that this disease is regional, nearly all cases occurring in Central Europe. Within ten years in Strasbourg, he has seen twenty-six cases, fourteen previously published from his department. The six cases presented in the present report were typical with one exception in which the lesions were situated on the right upper extremity. The sexes have been practically equally affected. In some of the cases, the disease has affected the trunk as well as the extremities, and for this reason he proposes to replace the denomination acrodermatitis with the simpler and more appropriate term dermatitis (dermatitis chronica atrophicans). The authors content themselves with a clinical description of their cases, reserving their detailed studies for special communications.

CAPILLAROSCOPY OF DERMATITIS CHRONICA ATROPHICANS AND SCLERODERMA. L. M. PAUTRIER and A. ULLMO, Bull. Soc. franç. de dermat. et syph. **36**: 776 (July) 1929.

In acrodermatitis chronica atrophicans there was an absence of the skin markings and a diminution in the number of capillary loops, while the subcapillary plexus was more distinct than normally.

In scleroderma there was a conservation of the normal skin lines, a decided diminution in the number of terminal capillary loops and areas of pigmentation and an absence of pilous and sudoriparous orifices.

ASSOCIATION OF ACRODERMATITIS CHRONICA ATROPHICANS AND SCLERODERMA. MAIRE and F. WORINGER, Bull. Soc. franç. de dermat. et syph. **36**:780 (July) 1929.

The patient exhibited acrodermatitis chronica atrophicans of all extremities, while the calves and thighs showed scleroderma. This condition was also present on the arms but to a lesser degree. There was an increased amount of calcium in the blood.

TUMOR FORMATION IN ACRODERMATITIS CHRONICA ATROPHICANS. DISS and WORINGER, Bull. Soc. franç. de dermat. et syph. **36**:783 (July) 1929.

In this disease true tumors are rare, the nodules commonly encountered being due either to collagenous or elastic tissue alterations or to inflammatory infiltrations. Histologically, the true tumors, have been fibromas, leiomyomas, histiocytomas or xanthomas. The case studied by the authors was a histiocytoma.

THE HISTOLOGY OF ACRODERMATITIS CHRONICA ATROPHICANS. L. M. PAUTRIER and A. DISS, Bull. Soc. franç. de dermat. et syph. **36**:785 (July) 1929.

The authors give a résumé of the histology of this disease. They have noted two conditions that have not previously been mentioned: (1) a sclerosis of the nerve fibers with increase in the cells of Schwann and fragmentation of neurokeratin (in the second stage), and (2) the muscles and hairs parallel the epidermis instead of ascending obliquely from the depths.

ETIOLOGY OF ACRODERMATITIS CHRONICA ATROPHICANS. FIDANZA, Bull. Soc. franç. de dermat. et syph. **36**:793 (July) 1929.

On account of the hypothesis that this disease was a syphilitic "endocrinid" (Audry), the author investigated the cases seen at Strasbourg for syphilis. No evidence of syphilis was found in any of the nine cases studied thoroughly from this standpoint.

ACRODERMATITIS CHRONICA ATROPHICANS TREATED BY SYMPATHECTOMY. R. LERICHE and R. FONTAINE, Bull. Soc. franç. de dermat. et syph. **36**:803 (July) 1929.

The patient was 12 years of age and presented typical acrodermatitis chronica atrophicans of the right leg of two and a half years' duration. A perifemoral sympathectomy was performed in June, 1925, by Leriche. From that time the process appeared to be arrested and there was great improvement in gait. The skin was more supple. In March, 1927, a right lumbar ramisection was performed. Since then there has been progressive improvement.

TREATMENT OF ACRODERMATITIS CHRONICA ATROPHICANS. NICOLAS and PÉTOURAUD, Bull. Soc. franç. de dermat. et syph. **36**:808 (July) 1929.

The authors achieved considerable improvement from the persistent application of thyroid and ovarian extracts and inunctions of cod liver oil to the affected parts.

HISTOLOGY OF ANETODERMA. L. M. PAUTRIER and A. DISS, Bull. Soc. franç. de dermat. et syph. **36**:815 (July) 1929.

From the histologic standpoint two groups of anetoderma can be recognized, one associated with acrodermatitis chronica atrophicans, the other an independent process. The authors report concerns the latter group. In this group they found a perivascular infiltrate in distinction to that found in Pick-Herxheimer's disease, in which there is a collection of histiocytes paralleling the surface. In anetoderma

the infiltrate is most pronounced in the depths of the cutis, and in this zone there is considerable destruction of collagen and elastic fibers. It is this destruction which explains the occasional "hernias of adipose tissue" that are found in advanced cases of anetoderma.

POIKILODERMA AND POLYMYOSITIS. PETGES, MANGNEAU, LECOULANT and DELAS, Bull. Soc. franç. de dermat. et syph. **36**:817 (July) 1929.

The authors describe a case in which poikiloderma was associated with myositis. The patient's general state was poor with febrile outbreaks and infections probably of streptococcal origin. Petges (with Clejat) published the report of a similar case in 1906.

TWO CASES OF POIKILODERMA. S. NICOLAU, Bull. Soc. franç. de dermat. et syph. **36**:823 (July) 1929.

Nicolau gave a detailed account of two cases of this disease. In one there was an associated polymyositis (sclerotic type) similar to the cases reported by Petges. The other was of the type described by Civatte under the title poikilodermie reticulée pigmentaire, which, to Nicolau, is not sufficiently distinguished to be separated from the poikiloderma of Jacobi.

In the discussion, Civatte admitted that the condition which he described was the same as the melanosis of Riehl. There was some doubt in his mind whether or not the latter was a variety of poikiloderma.

ATROPHODERMIE VERMICULÉE OF THE CHEEKS. P. VIGNE, Bull. Soc. franç. de dermat. et syph. **36**:852 (July) 1929.

The author describes a case of this disorder in which the follicular plugs and follicular keratoses observed in other cases were absent.

DISCRETE PIGMENTED ATROPHY. F. KOGOJ and K. FARKAS, Bull. Soc. franç. de dermat. et syph. **36**:855 (July) 1929.

The patient was a young woman who presented scattered brown patches, some with depigmented atrophic centers. According to the patient, the condition had been present since birth, without change. The authors discuss the nosology of the case in some detail and conclude that it should be classed with the nevoid group of pigmented atrophies.

THE SYPHILITIC ATROPHIES. G. MILIAN, Bull. Soc. franç. de dermat. et syph. **36**:865 (July) 1929.

Syphilis is capable of producing atrophy in each stage, the atrophies of the tertiary stage being more extensive, with a slow and progressive evolution. Milian calls attention to a type of syphilitic atrophy which has escaped recognition. He designates it white atrophy and it occurs in a discrete and a segmental form. The discrete variety is found usually on the legs and suggests the cicatricial relics of small ulcers. The segmental type is usually distributed on the feet or lower third of the leg. The skin is thin and habitually shows slight desquamation. Occasionally, small ulcers occur, but cede to specific medication.

POST-TRAUMATIC CUTANEOUS ATROPHIES. DU BOIS, Bull. Soc. franç. de dermat. et syph. **36**:871 (July) 1929.

Du Bois describes several cases of circumscribed atrophies which followed months or years after the injury. As an example, he mentions a case of morphea in which the lesions appeared on the flanks in areas subjected to pressure by corsets. His cases were atrophies, not scars, since there had been no preceding wound. In studying the etiology of so-called idiopathic atrophy, preceding trauma should be considered.

RAYNAUD'S DISEASE WITH SCLERODACTYLIA. PETGES, LECOULANT and DELAS, Bull. Soc. franç. de dermat. et syph. **36**:877 (July) 1929.

In a classic case, considerable improvement was obtained with pluriglandular opotherapy and injections of acetylcholine.

CONTRALATERAL DISTRIBUTION OF SCLERODERMA IN A CONGENITALLY SYPHILITIC PATIENT. G. PETGES, Bull. Soc. franç. de dermat. et syph. **36**:880 (July) 1929.

In a child, aged 5 years, Petges noted circumscribed scleroderma of the right side of the face and of the left trunk and extremities. The child had congenital syphilis and improvement was obtained by means of specific therapy. The distribution, presence of syphilis and response of the scleroderma to antisyphilitic treatment are interesting from the standpoint of the etiology of scleroderma.

SCLERODERMA. NÆGELI, Bull. Soc. franç. de dermat. et syph. **36**:883 (July) 1929.

About 1 per cent of the cases seen in Berne are scleroderma. Of the twenty cases studied, none gave evidence of syphilis, but a number showed an increased calcium content of the blood. No treatment was satisfactory.

SCLERODACTYLIA WITHOUT INVOLVEMENT OF THE HANDS. G. LÉVY and ZORN, Bull. Soc. franç. de dermat. et syph. **36**:888 (July) 1929.

Lévy and Zorn's patient presented scleroderma, which, beginning on the forearms, rapidly invaded both upper extremities. Twelve years previously, the patient had had an indefinite disturbance of the hands, which had disappeared at the time of presentation. The basal metabolism was distinctly increased.

FOUR CASES OF SCLERODERMA. HUFSCHMITT, Bull. Soc. franç. de dermat. et syph. **36**:892 (July) 1929.

Two of the patients presented disturbances of pigmentation in addition to disseminated scleroderma. Both disorders may be attributed to an influence of the central nervous system. Two of the cases showed a moderate increase in the basal metabolism, while in two the marked increase indicated definite hyperthyroidism.

SCLERODERMA WITH GOITER AND INCREASED BASAL METABOLISM. LORTAT-JACOB, FERNET and Y. BUREAU, Bull. Soc. franç. de dermat. et syph. **36**:906 (July) 1929.

A case of scleroderma chiefly affecting the face and neck is reported, accompanied by a basal metabolism of plus 45 per cent.

SUBCUTANEOUS CALCINOSIS OF THE FINGERS ASSOCIATED WITH RAYNAUD'S DISEASE: BIOCHEMICAL STUDY. R. J. WEISSENBACH, E. W. VIGNAL and C. O. GUILLAUMIN, Bull. Soc. franç. de dermat. et syph. **36**:910 (July) 1929.

About 1910, Weissenbach (with Thibierge) described calcinosis in scleroderma, and a number of cases have been reported since. The present case of Raynaud's disease with concretions is closely related to the previous studies. The patient presented the classic phenomena of Raynaud's disease with firm nodules that roentgenography showed to be due to a deposit in the subcutaneous tissue. Chemical analysis showed that the deposits were composed of calcium salts (72 per cent) and organic matter, chiefly lipoids (28 per cent).

SCLERODERMA WITH RAPID EVOLUTION: IMPORTANCE OF INITIAL AND LATE VASCULAR LESIONS IN THE STUDY OF SCLERODERMA. L. M. PAUTRIER, Bull. Soc. franç. de dermat. et syph. **36**:928 (July) 1929.

Pautrier reported in detail a case of morphea in a female on whom numerous lesions, widely scattered, appeared in the first year of the disease. An interesting observation was a plaque encircling the base of each breast. The development of the violaceous border was striking in all lesions. This violaceous border seems to vary in intensity with the activity or torpidity of the disease. In the present case, each lesion began as a violaceous patch, apparently simple vascular changes. Biopsy showed the rich vascularity of the violaceous border in contrast to the poverty of vessels in fully developed patches. Pautrier conceives that ischemia is a necessary precursor of the tissue change that produces the sclerodermic infiltration.

LINEAR SCLERODERMA WITH "WHITE SPOT DISEASE." PAYENNEVILLE and CAILLIAU, Bull. Soc. franç. de dermat. et syph. **36**:939 (July) 1929.

The authors report a case of the coexistence of these conditions.

RELATION BETWEEN "WHITE SPOT DISEASE" AND SECONDARY CIRCUMSCRIBED SCLERODERMA. PAYENNEVILLE and CAILLIAU, Bull. Soc. franç. de dermat. et syph. **36**:941 (July) 1929.

The authors record clinical and microscopic observations on seven cases of sclerous atrophy which fall into the category of "white spot" disease. The clinical picture in these cases was not uniform, but there was a constant evolution of the lesions toward the firm type of atrophy. The histologic picture, in most essentials, was that of "white spot" disease. In all of the cases biopsies showed the structure of a tissue which in its ultimate evolution leads to a cicatricial state.

Recent microscopic and microchemical studies of the authors led them to suggest certain hypotheses on the evolution of cutaneous atrophies. In its essentials, their hypothesis conceives of ferments with coagulative properties and others with lytic action. Normal tissues possess these ferments in equilibrium; in scleroderma or other firm atrophies, the coagulative ferments predominate; in anetoderma and lax atrophies, the lytic command.

A CASE OF SCLERODACTYLIA WITH GRANULOMA PYOGENICUM AND MONOCYTOSIS. J. PEYRI and C. CARDENAL, Bull. Soc. franç. de dermat. et syph. **36**: 953 (July) 1929.

The patient was a man, aged 67, with sclerodactylia and morphea. Granuloma pyogenicum appeared on the right wrist. Hemanalysis showed a monocytosis (48 per cent of mononuclear leukocytes) which, to the authors, is of significance since they have noted it in three other cases. Its significance seems to be related to the reticulo-endothelial system, probably an expression of functional inhibition.

PSEUDOSCLERODERMAS OF INFANTS. DISS and WORINGER, Bull. Soc. franç. de dermat. et syph. **36**:960 (July) 1929.

Diss and Woringer divide these disorders into three groups: (1) lipophagic granuloma, (2) sclerema and (3) true scleroderma. The first type is most common. It has been given a variety of names (subcutaneous adiponecrosis, Fettsclerose, etc.). Lipophagic granuloma is due to a change in the subcutaneous fat following obstetrical trauma. The indurations begin a few days after birth and disappear within three or four months. Histologically, the process is confined to the subcutaneous tissue. Anatomically, there is a decomposition of fats into fatty acids and these, acting as foreign bodies, provoke a foreign body reaction.

There is no accord concerning sclerema. Classic opinion admits an adipose and an edematous sclerema. Sclerema is a symptom of debility in the new-born infant and appears commonly in premature infants who have definite hypothermia. It is

fatal. The solidification of fats seems based on three factors: a special chemical constitution of the fats, hypothermia and dehydration. Scleredema is very rare, and the prognosis is not so grave as in the foregoing type. Its pathogenesis is not well understood.

True scleroderma occurs in infants, but is very rare. Most of the reported cases should be classed as lipophagic granuloma.

RELATIONS BETWEEN DERMATITIS CHRONICA ATROPHICANS, ANETODERMA AND SCLERODERMA. L. M. PAUTRIER, Bull. Soc. franç. de dermat. et syph. **36**: 973 (July) 1929.

From the clinical standpoint, these disorders present sensibly different features. But if they are analyzed from all aspects they will be found to have many close affinities.

In twenty-four cases of acrodermatitis chronica atrophicans, Pautrier found an associated anetoderma four times. Both conditions begin with inflammation, develop slowly and end with flaccid atrophy. Histologically they are closely kin.

There is also a close relationship between scleroderma and acrodermatitis chronica atrophicans. In twenty-four cases of the latter, sclerodermiform lesions were encountered in fourteen. Pautrier thinks that it is bandying words to designate the lesions as sclerodermiform; they are elements of scleroderma. The strict affinities of these three disorders can be understood better if they are looked on as disturbances of connective tissue metabolism rather than as independent pathogenic entities.

LESIONS OF THE SYMPATHETIC GANGLIONS IN SCLERODERMA. R. LERICHE and R. FONTAINE, Bull. Soc. franç. de dermat. et syph. **36**:982 (July) 1929.

In a histologic study of a number of ganglions removed at operation, Leriche and Fontaine found frequent pathologic alterations, but none of a specific character. Fibrosis, leukocytic infiltration and vascular degeneration of ganglion cells were encountered, but these are seen in other disorders. Even these changes were inconstant, since some of the ganglions were normal. In short, no lesions characteristic for scleroderma were noted in these structures.

BASAL METABOLISM IN CUTANEOUS ATROPHIES AND SCLERODERMA. L. M. PAUTRIER and J. BRUSSET, Bull. Soc. franç. de dermat. et syph. **36**:987 (July) 1929.

In ten cases of acrodermatitis chronica atrophicans, six gave normal figures, one increased and one diminished. Two cases of scleroderma showed normal and two increased figures.

BLOOD CALCIUM IN CUTANEOUS ATROPHIES AND SCLERODERMA. L. M. PAUTRIER and ZORN, Bull. Soc. franç. de dermat. et syph. **36**:991 (July) 1929.

In acrodermatitis chronica atrophicans the blood calcium was normal, while in scleroderma (six cases) increased blood calcium was the rule. On account of the small number of cases, definite conclusions were not permissible.

SYMPATHECTOMY IN SCLERODERMA. R. LERICHE and R. FONTAINE, Bull. Soc. franç. de dermat. et syph. **36**:995 (July) 1929.

The participation of the sympathetic system in scleroderma seems demonstrated by both the clinic and the laboratory. The authors' reasons for operative intervention are based on both grounds. Experiences with sympathectomy reported in the literature reveal both successes and failures.

Leriche and Fontaine have treated six patients with scleroderma by operations on the cervical sympathetic chain. Their first three patients, operated on four

years ago, now show definite improvement. In their last three patients, two show no effect so far, and one is still under observation.

From their collected and personal experience, the authors conclude that sympathectomy is beneficial in properly selected cases. Selection implies mainly early cases. Complete cure is not to be hoped for since the affected areas cannot return to a normal state. Amelioration and arrest of the disease have been accomplished. The authors discuss the type of operation; with lesions of the extremities, periarterial sympathectomy should be tried first; on failure of this, ramisectomy or ganglionectomy should be performed.

TWO CASES OF GENERALIZED ALOPECIA TREATED SUCCESSFULLY ON PHOTODYNAMIC PRINCIPLES. H. JAUSION, R. SOHIER and ANTONELLI, Bull. Soc. franç. de dermat. et syph. **36**:1187 (Dec.) 1929.

The authors' method consists in the intravenous injection of acriflavine (an acridine derivate with photosensitizing properties) followed by exposure to ultraviolet light. They give two detailed case reports, showing successful results in cases approaching alopecia universalis. They have treated sixty-one patients by this method with satisfactory effects. In the discussion, Pautrier mentioned that he had been disappointed in his therapeutic attempts with so-called photodynamic methods.

NONANESTHETIC LEPROMAS. GOUGEROT, BARTHÉLEMY and ARNAUDET, Bull. Soc. franç. de dermat. et syph. **36**:1210 (Dec.) 1929.

The authors report two cases of mixed leprosy in which normal sensation was present in the lesions. As other similar cases have been described, it is a mistake to rule out leprosy because anesthesia is not present.

PRIMARY ACTINOMYCOSIS OF THE GUMS. CHOMPRET and CROCQUEFER, Bull. Soc. franç. de dermat. et syph. **36**:1221 (Dec.) 1929.

Actinomyces were demonstrated in a case presenting gingivitis with shallow ulcers along the gum margins. In the discussion, Ravaut and Milian, after examining preparations of the organisms, questioned their identification.

BUCCAL LEUKOPLAKIA AND MELANOSIS. LORTAT-JACOB and LEGRAIN, Bull. Soc. franç. de dermat. et syph. **36**:1223 (Dec.) 1929.

The patient presented commissural leukoplakia and small melanotic patches on the buccal surfaces of the cheeks.

SPLENOMEGALY IN PRIMARY SYPHILIS. LOUSTE, Bull. Soc. franç. de dermat. et syph. **36**:1227 (Dec.) 1929.

Louste reported two cases showing these phenomena. He believes that splenomegaly is an important diagnostic sign and that it probably precedes the chancre. This clinical observation has been verified in monkeys. This splenitis in man may explain certain anemias, jaundice and albuminurias preceding or accompanying the chancre.

"LEUKOCYTO-REACTION" IN SYPHILIS. J. GOUIN, A. BIENVENUE, P. DAOULAS and M. PERES, Bull. Soc. franç. de dermat. et syph. **36**:1230 (Dec.) 1929.

The authors present, briefly, a new phenomenon in syphilis, which they designate "leukocyto-reaction." It seems to have diagnostic significance. (Their report in extenso is in process of publication.) Their observation of this reaction is an outcome of earlier studies on the leukocytic response to irradiation.

In all subjects, except syphilitic, it was shown that a leukocytosis or leukopenia promptly followed irradiation, the type of reaction depending on the region

irradiated. In syphilitic persons, leukocytosis always occurred. Following-up this observation, they have developed a test which seems to be specific for syphilis. It consists in a leukocyte count before and after autohemotherapy. Syphilitic persons show a prompt leukocytosis in this procedure; nonsyphilitic persons, leukopenia. The reaction may supplement the customary serologic procedures in syphilis. In certain circumstances (test of cure, early infancy), it appears to have advantages over the Wassermann and precipitation tests.

SURGICAL DIATHERMY IN THE TREATMENT OF SUBACUTE AND CHRONIC ADENITIS; ESPECIALLY IN BUBOS. RAVAUT and LANDOWSKI, Bull. Soc. franç. de dermat. et syph. **36**:1248 (Dec.) 1929.

Ravaut and Landowski have obtained satisfactory results by the use of this method. They coagulate the gland or fistulous tracts by the introduction of the needle at several points, thus producing gangrenous tracts which subsequently slough. Healing follows promptly.

KERATODERMA AND IRRADIATION OF THE PERIPHERAL SYMPATHETIC FIBERS. CHANTRIOT, Bull. Soc. franç. de dermat. et syph. **36**:1258 (Dec.) 1929.

Chantriot reports a case of keratoderma palmaris et plantaris of acquired idiopathic type which almost disappeared after several unfiltered irradiations to the axillary and inguinal regions.

SPOROTRICHOID TUBERCULOSIS. L. M. PAUTRIER and GLASSER, Bull. Soc. franç. de dermat. et syph. **36**:1093 (Dec.) 1929.

The patient presented a large lesion on the back of the right hand and wrist. This lesion had a papillomatous and verrucous surface. Echeloned along the arm were smaller gummous nodules. Fungi, however, could not be demonstrated. As the disease failed to respond to treatment for sporotrichosis, further investigation showed a tuberculous infection.

IMPETIGO HERPETIFORMIS. L. M. PAUTRIER, Bull. Soc. franç. de dermat. et syph. **36**:1104 (Dec.) 1929.

The author gives a clinical report of a case of this disease in a woman, aged 63. The disease first appeared on the breasts and pursued a slow but steadily progressive course.

FOUR CASES OF FAMILIAL XANTHOMA. HUFSCHMITT, Bull. Soc. franç. de dermat. et syph. **36**:1109 (Dec.) 1929.

In this family, four of five children were affected. The disease appeared between the third and fourth year. Each of the children had articular rheumatism about the tenth year. Examination of the blood in two patients showed hypercholesterolemia, hyperuricacidemia and hypoglycemia.

KERATOMA DISSEMINATA PALMARIS ET PLANTARIS (BRAUER-BUSCHKE). L. M. PAUTRIER and J. RŒDERER, Bull. Soc. franç. de dermat. et syph. **36**:1117 (Dec.) 1929.

The authors report a case conforming to the type described by Brauer and Buschke, except that it was nonfamilial.

DERMATITIS EXFOLIATIVE DUE TO AN ARTIFICIAL FERTILIZER CONTAINING CYANAMIDE. L. M. PAUTRIER, GASPART and ZORN, Bull. Soc. franç. de dermat. et syph. **36**:1166 (Dec.) 1929.

The patient was a farmer, who developed suddenly a generalized eruption of erythrodermic type. It was traced to contact with cyanamide.

MICHAEL, Houston, Texas.

Society Transactions

NEW ENGLAND DERMATOLOGICAL SOCIETY

RUDOLPH JACOBY, M.D., *Secretary*

Oct. 9, 1929

WALTER T. GARFIELD, M.D., *Presiding*

LUPUS VULGARIS. Presented by DR. CUMMINS.

K. S., a woman, aged 37, showed a condition the onset of which, about six or seven years before presentation, was marked by the presence of a small, scaly lesion on the nose. This lesion spread, and then healed slowly. The process repeated itself several times, up to the time of presentation. No pain was felt, only itching and burning when the lesion was active. No loss of weight or respiratory symptoms were present. The mother of the patient died of "bronchial trouble cough." The skin was generally clear except for the lesion on the nose. The chest was normal. The patient had had twelve radium treatments during the four years preceding presentation, the last of which was given in April, 1929.

DISCUSSION

DR. BOARDMAN: Beginning seven years ago — that is certainly an unusual case of lupus vulgaris. I could not find any lupus nodules, and one border particularly was slightly raised and nodular. I could not help thinking of epithelioma. I suppose a Wassermann test was made; but considering the age and the fact that there were no nodules, it occurred to me that epithelioma was a more likely diagnosis than lupus vulgaris.

DR. CUMMINS: The appearance of the condition has changed somewhat, I think, because of the treatment. The patient has had twelve radium treatments. I am not sure whether the Wassermann test has been reported on, but there is nothing in the history to suggest syphilis. The patient wanted to have some plastic work done, and she was sent here by her physician, in either Maine or New Hampshire, with the idea of having the condition curetted and prepared for plastic surgery. Then when she came in, the question of treatment was raised—whether or not it would be advisable to curet in a case in which so much tissue was broken down, especially at the end of the nose—and it was later decided to treat it by radium.

DR. TOWLE: Has the appearance of the lesion changed since the radium treatment?

DR. CUMMINS: We did not give the radium treatments. The patient came into the clinic and was sent into the ward and then she went away, and when she came in later, she had bronchitis and laryngitis. She has just returned.

DR. TOWLE: That is nearly a diagnosis of radium dermatitis, is it not?

DR. GREENWOOD: I agree with Dr. Boardman that it looks more like epithelioma.

DR. APPEL: I think it might be of interest in all these cases in which radiotherapy has been given, if possible, to give the data. It might have been of interest to know just how much radium this patient had had. It would make a difference in one's ideas about the cases if one knew these data and whether the radiotherapy consisted of roentgen-rays or radium.

DR. GREENWOOD: That would be all right if the data were given here or by the physician presenting the case, but if we have only the patient's statement, it is rather difficult.

A CASE FOR DIAGNOSIS. Presented by DR. CUMMINS.

L. G. C., a man, aged 29, born in Portugal, had his jaw fractured by flying rocks on Sept. 20, 1929, while blasting. There was no history of previous medication. On September 29, several pustules appeared on his face, but his temperature remained normal. On October 3, a slight elevation in temperature was noted. The lesions on the face were larger, and firm, reddened bases were observed. On October 5, a smear showed no recognizable organisms, and on October 7, the lesions on the face were smaller.

DISCUSSION

DR. OLIVER: It seemed to me possible that at the time of the accident, which was caused by blasting, there might have been some pebbles or grains of sand blown into the wound that might have given rise to this overgrowth of tissue. The patient has one lesion that I should like to curet to see what is at the bottom of it. I remember a similar case in which the condition looked like this, and with the patient under ether we dug out about a dozen little pebbles. I think there might be a foreign body, a bit of pebble, sand or dirt which might account for this appearance.

DR. TOWLE: I was much interested in it as being something or nothing. If I remember correctly, I noted on the consultation slip "actinomycosis? — blastomycosis? — eight days' duration." I could dismiss that, but I think Dr. Oliver's theory is the one most tenable. The patient told me that he was about 200 yards away from the blast, and that there was a shower of small dust and sand.

DR. MCCARTHY: The fact that the patient was 200 yards from the blast is rather against the foreign body theory.

DR. GARFIELD: His jaw was fractured as a result of the blast. If he fell down and hit himself hard enough to fracture the jaw, he might get some foreign bodies from the ground.

DR. BLOSSER: Do you think you could rule out blastomycosis?

DR. TOWLE: I think so. I do not think it would develop to that extent. It is not a particularly rapidly growing organism.

DR. BOARDMAN: If the face were shaved and ammoniated mercury put on, the condition might clear up. I think Dr. Oliver's suggestion is a good one.

DR. CUMMINS: The condition has improved a good deal in three days under treatment with simple boric ointment.

DR. MCCARTHY: I do not believe that the incubation period would be as short and that it would develop to any such extent in eight days, if the condition were blastomycosis.

SECONDARY SYPHILIS. Presented by DR. OLIVER.

A. A., a woman, aged 28, single, presented maculopapular lesions on the body and ring-shaped lesions on the face. There had been eruption on the face since Sept. 1, 1929, and two weeks following this a tonsillectomy and adenectomy were performed. The tonsils were sore at that time. A sore on the vagina followed the use of a strong douche about Aug. 1, 1929. A rash on the abdomen and at the same time over the chest and back was noted. The patient showed a definite coppery, macular eruption. Around the chin and over the cheeks there was a slightly raised, circular, ring-shaped eruption.

DISCUSSION

DR. OLIVER: She had a case of secondary roseola. I showed her because I thought the annular lesions were unusual in a white person, though one sees them frequently in colored persons. She came in the morning of presentation. No proof of the syphilis has yet been shown.

DR. DOWNING: I think she is the same woman who called us up. Her brother is a patient at the City Hospital.

DR. BOARDMAN: It was unusual to have the lesions only on one side; there was no symmetry of these lesions. That struck me as about as unusual as the ring-shaped lesion. They are almost edematous. The lesions I have seen in colored people have been more papular. These were really more like little wheals, and they pressed out so easily. It was unusual for syphilis.

DR. APPEL: Another interesting feature is the recent tonsillectomy and adenectomy. This is probably another case that we shall have to check up against the surgeons who operate on the throats of syphilitic patients.

DR. OLIVER: She had a lesion on the genitals, and she had a sore throat when the tonsils were taken out.

DR. APPEL: This makes me think of a case I saw at the Memorial Hospital a year ago. The condition was diagnosed as "Florida sore throat" by a physician in North Carolina; the patient was on his way up here. In Massachusetts it was diagnosed as tonsillitis, and he was given a date for a tonsillectomy and adenectomy, but the condition turned out to be secondary syphilis.

DR. OLIVER: I saw a patient with secondary syphilis who had made a date for a tonsillectomy. A peculiar condition was noted. The patient's Wassermann test showed strongly positive results, and it was afterward that he gave us the history of this infection in his throat as well.

GENERALIZED LICHEN PLANUS. Presented by DR. OLIVER.

An Italian woman, aged 55, showed a case of lichen planus of four weeks' duration.

DISCUSSION

DR. OLIVER: The condition began on the wrists, and only during the last two weeks has it spread rapidly over the body. A rather interesting fact in this connection was that her brother died about a week ago. She had been much worried, and immediately after his death, the condition began to spread rapidly. Lichen planus is sometimes thought to be due to overworry and nervousness.

DR. TOWLE: I was much impressed by the extent of the lesions. On the legs typical lesions were present. Had it not been for those lesions, I should have hesitated to make the diagnosis, as the lesions on the body were not typical.

CAVERNOUS ANGIOMA. Presented by DR. CHEEVER.

S. G., a white man, aged 36, showed a condition which had been present since early childhood. The distribution was on the jaws and on the tongue. A swelling caused marked distortion of the lower third of the face, that could be pressed into normal contour when the blood was forced out of the angioma. There was no change of color of the skin, but the mucous membranes were the bright red of angioma. This patient was operated on at the Boston City Hospital, with some temporary relief. This case was presented for suggestions as to treatment.

DISCUSSION

DR. OLIVER: I thought the condition looked angiomatous. Some cases of angioma we have had looked exactly like that. The patients have responded

fairly well to several doses of radium. I think radium would be indicated for the tongue. It might have a slow effect. I would not expect it to effect the rest of it because the distribution is too large.

DR. DOWNING: I saw that case in New York last week, and it caused an extensive discussion of radium. This case is like the one I showed a year ago in which Dr. Karzanjian did some plastic work; that case followed trauma. This case resembles it very much. I think there would be a good possibility of success in trying plastic surgery. There are no tissues that could not be removed, and I think that a large portion could be taken out. There are no large blood vessels there.

DR. OLIVER: We had one patient with a lesion on the neck something like the one in this case. The patient was a healthy child and almost died on the table.

DR. DOWNING: We took out a fairly large piece at the City Hospital with slight bleeding. Such lesions are mostly venous, and practically no hemorrhage results. A piece of a similar lesion was removed in which the patient had been unable to see out of his eye, and after removal of the piece, his eye opened and the edema disappeared.

DR. SWARTZ: I think Dr. Greenwood has the best suggestion: have the man grow a beard and leave the condition alone. It is benign. Why fool around with it when it is perfectly harmless?

DR. MCCARTHY: I am in favor of Dr. Oliver's theory. I have seen one similar case in which the patient was treated successfully with a few doses of radium. I have seen an extensive condition in a boy, aged 14, who had multiple operations. This lesion was as extensive as that of the man presented today; it extended well down the neck, and the cosmetic result was better than if it had been let alone. If a venous trunk is underneath, at this age, there will be much blood. I believe that this is a case for surgical measures, and that the tongue should be treated.

DR. CHEEVER: Dr. Blosser said he has treated a patient with a much less extensive but similar condition by cautery with practically no bad results.

LUPUS ERYTHEMATOSUS ON TATTOO. Presented by DR. APPEL.

A. M., a white, single seaman, aged 19, had a condition which had first appeared on the face seven months before presentation and had gradually progressed. None of the lesions had shown any tendency to heal. Examination showed a typical lupus erythematous eruption of the "butter-fly" type on the face, involving the nose and both cheeks; a few small, discoid lesions on the right arm and on the left forearm, lesions involving a tattooed design, with only the red ink areas affected. (The blue ink design was done four years before presentation, including a small spot of red at the base. The rest of the red was done three months before presentation.) Previous treatment with Kromayer's lamp and roentgen rays had had no obvious effect. The chief points of presentation were: development of lupus on the face of a seaman (exposure to elements); and development of subsequent lesion at the site of trauma (tattooing skin).

DISCUSSION

DR. TOWLE: This case suggests the old dictum in the treatment of lupus erythematosus: hit it hard or let it alone.

DR. STANDISH: What is this dye that was used?

DR. APPEL: In this case, the original design was put on four years previously, all in blue with one small place in red. The patient had no more tattooing done until three months before presentation. By that time, lupus had already developed on his face and arm. Three months before presentation, he had the background of the design (a picture of a tombstone surmounted by a cross) and the flowers

at the base of the design filled in with red tattoo. The lupus developed in all the new red areas, but not in the old original red area, showing that the element of trauma was the important exciting factor rather than the dye itself.

The patient is now under treatment with intravenous gold and sodium thiosulphate, and there is a definite, progressive improvement in all the lesions.

PROBABLE DRUG RASH. Presented by DR. CHEEVER.

H., a negro laborer, aged 45, whose history was hard to obtain because of language difficulty, seemed to believe that he had inherited a skin disease which worried him because it had never broken out in all these years. He went to a colored "professor" who gave him black pills, with a promise that he would break out and be entirely relieved. He was delighted when the rash was nearly black and matched the pills. The rash appeared eight weeks after he had first begun to take the pills, and was of four weeks' duration. The distribution was all over the body. The lesions were irregularly shaped areas as large as 1½ inches in diameter; they were nearly black with slightly raised, lighter colored borders. The patient's skin was moderately dark brown, and the face and lower arms were much darker than the rest of the body.

DISCUSSION

DR. OLIVER: One interesting thing was the lightness of the skin on the patient's body in comparison with that on his face. It looked like a marked depigmentation. The lesions looked more like those of lichen planus. The patient's right eyebrow was rather sparse, and I thought of the possibility of his being a leper, particularly as he came from New Brunswick where this condition is common. The pieces of tissue excised might show that condition. We had one patient with lesions that looked something like those in this case. The biopsy showed the lesions to be packed with leprocal bacilli. I think it is barely possible that something like that might be shown on further examination. It might account for the depigmentation of the body. Leprosy does queer things.

DR. STANDISH: On the chest were three atrophic lesions with raised borders. I wonder if it is an atrophic type of leprosy.

DR. TOWLE: Was there a distinct hemorrhage in those lesions?

DR. OLIVER: I do not think so. His face was black in comparison with his body.

DR. KARCHER: I do not think there is depigmentation. He said there had always been a decided difference between the color of his body and that of his face.

DR. STANDISH: Is that not a rather common thing in some of these semicolored persons?

DR. SWARTZ: I thought that the primary lesions on the forearms were angular, lichenified and shiny. That would point toward the diagnosis of lichen planus. The only thing against this diagnosis was the absence of itching. I questioned him, and he said that he did not have much itching.

DR. BOARDMAN: We had two cases of typical lichen planus. Everybody else on the staff laughed, and said I should not call it that as the lesion in the lichen planus did not cause itching. I looked it up in a great many books and found one that said itching was a variable symptom, often missing.

LELOIR TYPE LUPUS VULGARIS? Presented by DR. GREENWOOD.

LUPUS ERYTHEMATOSIS?

CONGENITAL SYPHILIS?

M. C., a woman, aged 65, a housewife, born in England, had a garland of lesions of four years' duration stretching across her forehead. They were super-

ficial, atrophic at the centers and infiltrated at the periphery, and they tended not to be round. The Wassermann report gave strongly positive results in April, 1927. A history was given of congenital syphilis. There were no signs of congenital syphilis at this time. Some specific treatment was given. The x-ray picture of the teeth was normal. The Wassermann test gave negative results in March, 1929. On Oct. 2, 1929, the Wassermann and Hinton tests gave weakly positive results.

DISCUSSION

DR. GREENWOOD: That patient was presented for the skin lesions as probably having lupus vulgaris of the leloir type. The positive results of the Wassermann test if that were a congenital thing, caused the impression that the lesions on the face were syphilitic. That border, with pressure of the glass, gives typical brownish papules. If it is lupus vulgaris of the leloir type, it is unusual enough to mention it here. I do not remember having seen that type here often. At one time at a clinic in San Francisco, five patients were shown with such conditions. I am sure it is not nearly so common here.

DR. TOWLE: I discarded the theory of syphilis on account of the appearance of the lesions, and I rather incline to the idea that it is a straight lupus erythematosus.

DR. GREENWOOD: The Wassermann test, though positive at the time of presentation has been changed to negative, with no change in the lesions, and with no intravenous therapy; the treatment has been only by mouth.

EPITHELIOMA? Presented by DR. OLIVER.

K. D., aged 52, a housewife, born in Ireland, presented a condition of twelve years' duration. There was a lesion on the left side of the face from the outer corner of her eye to the alae nasi. There was one scattered area with several superficial ulcerations. The scars were thick, and the patient said that they came from previous cauterizations. In 1927, she was sent to the x-ray department for treatment of ectropian and was advised against therapy. Plastic surgery was recommended. In 1929, crusts and scarred tissue edges in many places had a pearly border. The biopsy showed a probable case of epithelioma.

DISCUSSION

DR. OLIVER: I asked the patient to come in. She had been coming here for years; epithelioma has never been diagnosed before. On examining her here the other day, I found this border, and a case of epithelioma was proved by biopsy. The condition has been treated as lupus. I could not see anything that resembled lupus. The plastic surgery was done by Dr. Kazanjian. There is no evidence of lupus. The only activity left, I think, is at the borders. The rest is all cicatrized. I think it is just as well to let her alone. The disease is spreading slowly, and she will probably die of old age before it bothers her much.

A CASE FOR DIAGNOSIS. Presented by DR. DOWNING.

H. H., a woman, aged 60, had always enjoyed good health. One year before presentation she had a fibroid removed from the uterus. She had two children living and well, and she had had about twelve miscarriages. About one year before presentation reddish, slightly raised lesions began to appear on the bridge of the nose, extending to either side of the nose. These lesions had persisted. The Wassermann reaction was negative.

DISCUSSION

DR. GREENWOOD: I thought it was a case of sarcoid.

DR. TOWLE: I think sarcoid is the probable diagnosis, without a microscopic examination.

DR. MCCARTHY: That might not help.

DR. DOWNING: I thought it was a case of lupus erythematosus.

DR. GARFIELD: I was inclined to think so when I first saw it; sarcoid did not come to my mind. The slight scaling, as well as the location, suggested lupus erythematosus to me. Since I have heard the question raised as to sarcoid, I am not prepared to dispute it.

DR. TOWLE: One does not often find such a thick pile of masses as this in patients with lupus erythematosus.

BLASTOMYCOSIS. Presented by DR. SWARTZ.

A German machinist, aged 24, entered the Beth Israel Hospital four weeks previous to presentation, complaining of a rash. His family and personal histories were normal. Ten weeks before entry, the patient began to suffer from inflammation of the distal portion of the penis. The last exposure was five and one-fourth months ago. Eight weeks before entry, a physician withdrew blood from a vein, and reported that the blood was normal. A few days later the patient entered the Peter Bent Brigham hospital, was circumcised and was discharged in a few days with a wound which continued to show purulent inflammation thereafter. Six weeks before entry, the patient first noticed small, red papules on his forehead, and soon thereafter similar larger lesions appeared, scattered over the entire body.

A physical examination at the time of entry showed scattered, deep red, pigmented papules, as large as a few centimeters in diameter, with crusted surfaces, over most of the body, including the shaft of the penis. On the scalp there were a few large, fungating lesions, with epidermal abscesses, and circumscribed by a papular border. The glans and corona of the penis were covered with purulent exudate under which was a superficially ulcerated surface. Both tonsils were large and were covered with a grayish membrane, which, on being scraped away, revealed a superficially ulcerated surface.

Two dark-field examinations of the penile lesions gave negative results. Culture of the tonsils showed no Klebs-Löffler bacilli or Vincent's organisms. Direct smears of the scalp and penile lesions showed typical blastomycetes. Microscopic examination of a section of a skin papule showed blastomycosis. The urine and stool were normal. The white blood count ranged from 13,500 to 17,600, with from 12 to 15 per cent eosinophils. The Wassermann test of the blood and the Kahn and Hinton tests had given strongly positive results on two occasions during the month before presentation.

The patient received twenty-four inhalations of ethyl iodide, each of from 2 to 8 Gm.

DISCUSSION

DR. TOWLE: I was interested in comparing the case presented with those which were here before the World War. There were a series of three, I think, in which the lesions were not of this exudative, oozy type, but were more like lupus erythematosus — ulcerated but never oozy. They were demonstrated by the microscope. This case seemed much more florid than those that I have been accustomed to see. I wondered if there had been anything in the treatment to cause it; if there had been any external treatment.

DR. SWARTZ: Some grease has been used and some boric acid, and within the last week, a little sulphur. Dr. Cheever saw the patient on his first visit. Then the lesion was much more papillomatous; one could squeeze any of them and get pus, more markedly along the border, whereas now it is receding, and the border is clear.

At Dr. Towle's suggestion, Dr. Swartz was asked to demonstrate his ethyl iodide apparatus; the secretary first read a summary of the case.

DR. SWARTZ: My theory was that iodide was the proper drug to use, and I felt it was not given in concentrated enough doses and the problem was how we

could give more concentrated doses. Also the route of the infection was studied, and especially the work done by Freed and others led me to believe that many of these conditions are not only local infections but also hematogenous, and for direct proof of that, introducing iodide would probably be enough. Together with Dr. Blumgart we worked out a method of inhalation whereby we can give iodide in concentrated doses by getting it into the pulmonary circulation. The next problem was which drug could be inhaled. Ethyl iodide had been used for the study of blood flow by Dr. Henderson and Dr. Blumgart, and we decided to try it on these. The next problem was to get up an apparatus whereby we could administer this treatment, and I think I can explain this easily (explanation of mechanism). We have had no ill effects from it. In one or two cases, the patient got drunk by it, but on getting out into the open, the drunkenness disappeared. I have used this treatment now in practically every mycotic infection. The results are varied but altogether encouraging. In this case of blastomycosis I can refer to Dr. Cheever because he saw the patient before the treatments were given. The patients respond faster with the first twelve treatments; after that it is slower. I have had two cases of favus. One case of favus I have looked at was absolutely negative on microscopic examination. That patient was a child 7 years old who had had twenty inhalations and was normal after twelve. We decreased the doses, and there was a slight recurrence; we resumed the treatments, and the tests now show negative results, and the scalp is clear except for slight scars. We had a case of favus in which the condition was epilated by the roentgen rays with recurrence. After twenty-four inhalations she showed no active lesions. Epidermaphytosis of the perineal region had been treated. These patients responded rapidly. I recall one case in particular. The patient had been everywhere; finally he went to the Long Island Hospital, stayed there awhile and was sent to the Jewish Chronic Hospital, where I treated him by inhalation. He responded to the second treatment and has continued to respond with slight recurrences until twenty inhalations had been given. He is up and around and out of the chronic hospital. The difficult cases are those of epidermaphytosis of the hand. The lesions clear rapidly at first; then they are slow to respond. Of course, patients wash their hands and handle things, and that affects the response. The treatment has been tried on patients with cryptococcosis epidermica. A young girl was practically cured. I have seen much better response to this treatment than to any local treatment or to any other type of treatment that I have followed until now, and I think it is somewhat encouraging. The treatments are given practically daily; then every other day. The children are given smaller doses, starting with 1 grain (0.065 Gm.) and working up to 2 grains (0.13 Gm.). I have not given any children more than 2 grains (0.13 Gm.) at a single dose.

DR. GRUND: Why is this treatment better than when iodide is introduced by mouth?

DR. SWARTZ: I can explain that only by saying that there is a good deal wasted in that treatment; one is not able to give as concentrated doses. Furthermore, it seems to work better than intravenous treatment. I can explain it only by saying that it is a more direct route. The reports of introduction by the intravenous method have not compared with inhalation. Perhaps the coefficient of absorption of the lungs is greater and a greater amount is inhaled.

DR. GRUND: What proportion of iodide rash is one apt to get? How does that compare with the mouth method?

DR. SWARTZ: I do not think one can measure that. A person can get an iodide rash with 10 grains (0.65 Gm.) as well as with 50 (3.25 Gm.), if he is susceptible. I have had patients with an iodide rash with 2 grains (0.13 Gm.) and patients who have not had it with 50 grains. If it is a slight rash, it is insignificant, and I continue the treatment. If it is severe, I stop it for a few days. Some work is being done now on the blood content, and also on the urine and saliva, to find out just what happens to the ethyl iodide in these cases of rash. Judging from the disappearance of the iodide rash, it is eliminated rather rapidly.

DR. CHEEVER: We had a man who got a rather severe rash with from 5 to 10 grains (0.32 to 0.65 Gm.) given intravenously, and the dose was raised to 15 grains (0.97 Gm.) three times a week under this ethyl iodide, and the blastomycosis has improved rapidly.

DR. GRUND: What is supposed to be the action on the organism itself?

DR. SWARTZ: I have not studied that; I cannot answer now.

DR. DOWNING: A thing which impressed me in at least two cases in two women with extensive paronychia was that the condition cleared up completely without any further treatment. After saying a word of praise for Dr. Swartz in this work, I would like to disagree with him on this case. I would be more inclined to think that this is a case of syphilis. The lesions themselves resemble a case of blastomycosis that I saw, but still I have not had demonstrated to me anything that looked like blastomycosis today. I think the treatment with ethyl iodide would naturally improve syphilitic conditions. I am more inclined to think this is a case of secondary syphilis than blastomycosis.

DR. SWARTZ: I think Dr. Downing has made a good point, because that is what all of us thought, but if Dr. Downing had seen the case at the beginning, even clinically, and had seen the typical papillomatous border and these epidermal abscesses and the blastomyces, which one does not see in secondary syphilis, he would be immediately convinced that it is not syphilis. As to the organism, this slide was taken after the patient had had six inhalations. Unfortunately, we could not keep the pus smears, but they showed typical budding blastomycetes.

DR. MCCARTHY: I should like to ask whether any intravenous treatment has been given?

DR. DOWNING: I should be interested to know what intravenous treatment would do. Why not give six intravenous treatments of arsphenamine?

DR. SWARTZ: Arsphenamine has been used in blastomycosis with reports of some good results.

DR. BENNETT: I understand both the Wassermann and the Hinton tests gave positive results. What that the original Hinton test or the modified?

DR. SWARTZ: The Wassermann and Hinton tests have given strongly positive results on two occasions during the past month.

DR. BENNETT: It seems to me this is an illustration of the fallacy of paying much attention to the Wassermann or Hinton tests. Many writers are of the opinion that the Wassermann test is absolutely of no use. I have recently been to the Hinton laboratory, and there are a number of cases there on which research work is being done. In one series the Wassermann test was positive in twelve cases; the Kahn, positive in thirteen and the modified Hinton in twenty-five cases; and that was followed up with another series.

DR. BOARDMAN: Contrary to that, we have been doing the Kahn, Wassermann and Hinton tests and have found the Hinton the least satisfactory of the three. The laboratory workers have been out to Dr. Hinton's laboratory and have tried to get the method of reading the reactions, and they still insist that it is a hazy thing, and they have practically decided to give it up at the City Hospital. We have not had much luck with it. The Wassermann and Kahn test are both good; one reacts one time and the other another, and there does not seem to be any rime or reason about it, but I would not want to see either of them given up. We are much better off with two reactions than we were with one.

DR. BENNETT: I am contending for relying on but one histologically, but I am contending for a modified Kahn or a modified Hinton against the old Hinton and Wassermann tests.

DR. GRUND: There is no reason why this patient cannot have secondary syphilis with the blastomycosis.

DR. DOWNING: How do you explain that condition of the throat?

DR. SWARTZ: There have been cases of blastomycosis reported with descriptions similar to the lesions found in this throat and in the ulcerations. I could not prove microscopically that the condition in the throat was blastomycosis. The smears from the throat gave negative results. There is a picture of Castellani's of mucous membrane lesions similar to the lesions seen in this case, only involving the lower lip rather than the tonsils. There is also a blood culture. I feel that this man has not only a blood mycosis but a generalized systemic blastomycosis.

DR. DOWNING: Has there ever been a patient with systemic blastomycosis who looked as well as he does?

DR. SWARTZ: He has had good treatment.

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY

MAX SCHEER, M.D., *Secretary*

Meeting, Nov. 6, 1929

FRANK H. FRASER, M.D., *Chairman*

LUPUS MILIARIS DISSEMINATUS FACIEI (?) Presented by DR. ROSTENBERG.

A woman, aged 43, the mother of two healthy children, had no personal or family history of tuberculosis. She dated her present skin eruption to an attack of parotitis, after which the skin of both cheeks had appeared wrinkled. Soon thereafter the skin eruption appeared on the right cheek, spreading over the entire cheek on both sides and also involving the chin. No other part of the skin was affected. The rash consisted of closely grouped and disseminated bright red and paler papules, varying in size from that of a pinhead to that of a millet seed. There were a few telangiectases over the cheek bones. Here the lesions appeared in plaque form. The discrete lesions on the chin appeared somewhat translucent and more yellow. On diascopic examination, they looked like yellowish dots.

DISCUSSION

DR. WISE: I think that the clinical picture is one of cutaneous tuberculosis and corresponds to the original description of "acne telangiectodes," rather than disseminated lupus miliaris.

DR. WOLF: In view of the fact that one cannot get a biopsy, would it not be advisable to apply a therapeutic test with a gold compound and sodium thiosulphate and have the patient presented at a future time?

EPITHELIOMA—BASAL CELL. Presented by DR. FEIT.

Mrs. A. M., aged 40, exhibited a tumor of twenty years' duration. Extending along the lower border of the left eyelid, examination showed a hard, fibrous tumor, about the size of a lima bean, with an irregularly outlined, ulcerated surface covered with a dark brown crust. On the upper two thirds of the conjunctiva were a sharply defined infiltration and redness. No glandular involvement was noticeable. The patient also showed numerous seborrheic warts and pedunculated fibromas, the size of a hazlenut, on the back.

DISCUSSION

DR. ELLER: I think that plastic surgery in this type of case is preferable to any other form of treatment, as the lesion involves the mucous membrane as well as the skin.

DR. LEVIN: I have had the pleasure of witnessing Dr. Wyeth operate on similar lesions by means of surgical diathermy, and have observed the excellent results that he obtained. I think that we ought to call on Dr. Wyeth to discuss the treatment for this type of lesion when occurring on the eyelids.

DR. WYETH: I recommend the lighter monopolar current to desiccate this lesion. Monopolar electrodesiccation is done with a current of high voltage and low amperage and therefore does not penetrate into the depths of the tissues. It is a simple matter to desiccate such lesions and curet them away, and that is the only method I know of that will heal up without scar formation. For this reason I do not believe that the results of plastic surgery would be as good.

DR. ANDREWS: I had this patient in consultation last week with a plastic surgeon and with Dr. Whipple. They did not advise surgical intervention because it would leave considerable scarring and deformity.

In regard to surgical diathermy, I do not think that anything could be accomplished by that method that would not be accomplished by surgery. I treated the lesion with the roentgen rays and will show the patient again in two months. I think that the lesion will heal with less scarring handled by that method than by any other. I think that radium would accomplish the same result, but the patient cannot afford radium.

DR. ROSTENBERG: I had a similar case in which the lesion was situated on the inner canthus of the left eye. I used electrodesiccation, followed by two units of the roentgen ray, with a most gratifying result.

DR. WOLF: I was surprised to hear Dr. Eller suggest surgical treatment. A year ago he presented a case of epithelioma of the upper eyelid in which the patient was treated with the Grenz ray and was apparently cured.

DR. ANDREWS: We have Grenz ray machines, but do not consider the method worth very much. The Grenz rays are mostly absorbed in the first 2 or 3 mm. of skin.

DR. ELLER: Regarding Grenz rays, they are soft roentgen rays with very little penetration. They have been found useful in the treatment for multiple flat epitheliomas of the skin, but not of the lower eyelids. I have had satisfactory results with some lesions of the upper eyelids, and failures with others. These rays are beneficial in the treatment for young keloidal scars, also in folliculitis of the scalp.

Regarding the epithelioma, which in this case involves the mucous membrane of the lower lid, I think that it is dangerous to depend on any form of irradiation in that area. I would like to see more five year cures with the roentgen rays before I would advise the treatment of lesions on the lower eyelid with the roentgen rays or radium.

DR. ANDREWS: We have always considered the roentgen rays rather a good treatment for basal cell epithelioma, and reports of clinical results have been splendid. I am rather surprised to hear it condemned as a treatment for basal cell epithelioma. I do not see any reason why irradiation should not be applied in this location as well as in any other. The eyeball is shielded by a plate of lead covered with paraffin. The conjunctiva is anesthetized and there is no trauma. If the eyeball is protected, I can see no danger.

DR. BECHET: Basal cell epitheliomas are not always easy to cure. At times I have seen them grow and spread most rapidly. Occasionally, prickle cell epithelioma may begin on the basal cell type. I recall a large, typical, flat, superficial epithelioma on the forehead, in the center of which was a cauliflower-like mass. Sections from different parts of the lesion demonstrated basal and prickle cell types.

As far as treatment is concerned, simple curettage will do very well, provided the curet is sharp and the operator is willing to curet with energy. The use of acid nitrate of mercury after curettage is especially valuable, and the cosmetic results are fully equal to, if not better than, many of the new procedures. The

originator of the method, the late Dr. Sherwell, was especially enthusiastic. His experience with it was vast and extended over many years.

DR. WYETH: Basal cell epithelioma is not always benign. I have often known it to cause death, and I know of nothing so badly bungled by the dermatologist as basal cell epithelioma. Some cases respond well to irradiation, but many others do not. For the physician to persist in irradiating in these unsuccessful cases reflects neither credit to himself nor fairness to his patient. I believe that within two minutes we can destroy with surgical diathermy what it would take two months for the roentgen rays to accomplish.

DR. OULMANN: I would like to refer to a case of multiple basal cell tumors, starting at the border of the mucocutaneous juncture of the anus. The case came to autopsy in time. Dr. Fraser, who saw the specimens, regarded the case, which had metastases all over, as an unpigmented melanoma, while others regarded the condition as a basal cell epithelioma with metastases. Such cases are reported, and I state these facts because I believe that basal cell epitheliomas at the mucocutaneous border ought not to be taken too lightly.

DR. GROSS: Epithelioma of the canthus often does not respond well to roentgen or radium therapy. The lack of underlying tissue providing secondary irradiation or cellular reaction may be responsible for some failure of irradiation in this location and in others, as the ear and forehead. Lack of response should always be a warning to desist in the use of the roentgen rays in these cases.

DR. FEIT: I think that the kind of treatment should depend on the type of lesion. In my opinion, most of them are squamous cell carcinomas, because of their location on the mucocutaneous surface. We have heard so much lately about basosquamous cell epitheliomas that the clinical appearance alone is not sufficient. I should think that the best thing would be to have a biopsy done and then determine the form of treatment.

DERMATITIS VENENATA (INSECT POWDER). Presented by DR. HOPKINS.

Mrs. A. H., aged 59, Irish, a housewife, was admitted to the Vanderbilt Clinic on Sept. 18, 1929, with an itching eruption on the face, neck, upper extremities and trunk of fours days' duration.

Four days prior to presentation the patient had sprayed her bed with an insecticide ("J-O") and had slept in the same bed twelve hours later. During the night, she awakened with an intense itching and burning of the face and neck. By morning these areas and the upper part of the trunk were covered with a rash, resembling measles. Within the next two days her eyelids became swollen and shut and the face was covered with an "oozing eczema." On the fourth day the patient was admitted to the Vanderbilt Clinic.

Examination of the areas involved showed a diffuse erythematovesicular eruption on an acutely inflamed skin, with edema of the eyelids. With the application of calamine lotion and the avoidance of insecticides the eruption cleared up within a month. At the time of presentation the skin was entirely normal.

The patient gave a history of having had a similar eruption on the face and neck five years previously. Her pharmacist had prescribed a lotion and told the patient to stop wearing a dyed fur collar. She did this, and the eruption promptly cleared up. She had worn a dyed fur collar later without causing an eruption.

The patch test with the patient's fur collar was negative. Patch tests with 10 per cent paraphenylendiamine gave a marked erythema with induration within twenty-four hours. This persisted for about ten days. The patch test with "J-O" insect powder gave marked erythema with minute vesicles in the area, and surrounding it there was also a local increase in the temperature and tenderness on pressure. The reaction persisted for two weeks.

The scratch tests with pyrethrum, 10 per cent paraphenylendiamine and "J-O" gave no immediate reactions, but the "J-O" gave a positive delayed reaction. An intradermal test with pyrethrum was negative. Patch tests of paraphenylendiamine

and "J-O" were repeated two days before presentation (November 4) and showed the following results: (1) paraphenylendiamine erythema with vesiculation and induration and (2) "J-O," erythema with induration.

DISCUSSION

DR. HOPKINS: This patient was presented to show the influence of skin tests in the diagnosis of dermatitis venenata.

DR. GOODMAN: I am happy to see this case and the tests which have been made. I often encounter a patient with dermatitis who has had some hair dye applied. It is often taken for granted that the hair dye is at fault.

My tests with paraphenylendiamine, using the scratch method, have not been very conclusive. It is advised in practically every book of directions before the use of the hair dye, but very few operators use it. In this instance, the absence of the tests for paraphenylendiamine and the presence of the positive test for "J-O" powder should be conclusive.

DR. HOPKINS: I do not think that the scratch test is worth much for testing for external irritation. It is necessary to put on the suspected irritant under an adhesive patch and observe the effect after twenty-four hours. Dr. Kesten has done a series of seventy such tests with 10 per cent paraphenylendiamine. Only four patients reacted, and all of these had or gave a history of a dermatitis due to this dye. This shows that a positive reaction to a 10 per cent solution indicates sensitization to paraphenylendiamine and is of some diagnostic importance.

SARCOID? Presented by DR. CANNON.

Mrs. I. K., aged 38, a Russian, was readmitted to the Vanderbilt Clinic on Oct. 16, 1929, with a tumor on her forehead. A similar lesion had been excised in 1926. At that time a clinical diagnosis of multiple benign cystic epithelioma was made. The microscopic diagnosis was sarcoid of the Spiegler-Fendt type. Histologically, the section showed some edema and atrophy of the epithelium. The main changes, however, were in the corium, which was edematous and showed newly formed fibroblasts and nodules of infiltration about the sweat ducts, follicles and vessels. These infiltrations consisted of a variety of cells: fibroblasts, plasma cells, many large leukocytes and large cells with lobulated nuclei, and some had inclusion bodies that were basophilic. Multinucleated cells were seen in some of the sections. The changes found were definitely granulomatous, and most nearly resembled those seen in lymphogranuloma. The most likely diagnosis seemed to be lymphogranuloma.

One year before presentation a similar tumor began to develop on the forehead just to the right of the midcenter, which slowly increased in size. The patient was referred back to the Vanderbilt Clinic through the courtesy of Dr. Lapowski.

In 1927, physical examination showed a chronic cardiovascular disease with probable mitral insufficiency. The Wassermann test, urinalysis and examination of the sputum gave normal results at that time. On April 11, 1927, a roentgen examination of the lungs showed an "increase in hilus shadows and fine lines of peribronchial infiltration, especially in the right upper lobe. There was not sufficient evidence to diagnose tuberculosis. The heart shadows were suggestive of mitral disease."

On Oct. 8, 1929, reexamination of the patient showed a clear skin except for a tumor over the right frontal region 2 cm. to the right of the midline in the center of the forehead, and symmetrical with the scar of the previous lesion there was a tumor 1 by 0.5 by 0.5 cm., which was oval with an irregular border, red, smooth and glistening and had two venules running across the surface. On diascopic pressure the tumor became colorless and seemed to be made up of two coalesced tumors with a third almost discrete smaller tumor at the lower border. There was no tenderness or inflammation. The scar (the site of the previous excision) showed no recurrence. There was no lymphadenopathy.

Roentgenograms of the femur, humerus, hands and spine, made on October 8, were normal.

The blood count taken on October 15 showed 9,500 white cells, 50 per cent polymorphonuclears, 48 per cent lymphocytes and 2 per cent eosinophils. The tuberculin test made on October 25 (intradermal, 1:10,000 and 1:1,000) was negative.

DISCUSSION

DR. FEIT: We observed a similar case which we thought was sarcoid, in which biopsy showed leukemia of the skin.

DR. HOPKINS: The cells were not quite uniform enough in this case to suggest leukemia.

DR. GOODMAN: The patient was seen some years ago at the New York Skin and Cancer Hospital. We learned subsequently that the lesion had been removed and that the histologic diagnosis had been sarcoid. The clinical diagnosis made had not been sarcoid, but some form of endothelioma. The patient now presents a lesion that is very much the same as that seen four years ago.

DR. ELLER: About four years ago we saw this patient with a lesion on the upper part of the forehead. The lesion was flatter and more reddish. I believe that at that time Dr. Satenstein made a diagnosis of sarcoid from a microscopic study.

DR. CANNON: This patient had practically the same type of lesion removed at the Vanderbilt Clinic three years ago, and the histologic diagnosis then made was the Spiegler-Fendt type of sarcoid. The lesion has recurred during the past six months and this time we thought it was one of simple sarcoid, probably of tuberculous origin. I also thought that the arrangement of the tumor was that of sarcoid, although the infiltration suggested lymphogranuloma. It would be unusual for a person to present an isolated skin lesion of that kind and have it recur in the same location three years later after a lapse of three and one-half years, without evidence of a general dissemination in the internal organs or glands. I think that this benign tumor is more likely sarcoid than lymphogranuloma.

NEURODERMATITIS VERRUCOSA. Presented by DR. GROSS.

M. S., a white man, aged 22, was first seen on Oct. 16, 1929. He gave a history of having had an eruption for two and one-half years which was so itchy that he had not been able to work. The condition had started on the legs shortly after a severe fright. At that time he had received injections of mercuric salicylarsenate and arsenic in different clinics for lichen planus.

On examination, numerous patches of different sizes were found on the anterior surfaces of the legs. These patches were lichenified and pigmented. There were a number of discrete, nodular, violaceous lesions with a slightly verrucous surface. On the arms and thighs were several circumscribed areas of thickening and marked criss-cross lining of the skin, pigmentation and excoriations. The diagnosis of neurodermatitis was made. A tar ointment had caused considerable improvement.

The patient was presented because of the great resemblance of some of the lesions to prurigo nodularis, to demonstrate the difficulty of differential diagnosis of neurodermatitis and lichen planus hypertrophicus of the legs, in the absence of lesions in other parts of the body, in consideration of a possibly purely neuropathic etiology of certain cases of neurodermatitis.

DISCUSSION

DR. OULMANN: I saw this patient about a year ago. At that time he had typical lesions of lichen planus with some lesions in the mouth. My diagnosis was lichen planus verrucosus.

DR. ELLER: I think that this case is fairly typical of lichen planus hypertrophicus.

DR. FEIT: The case probably was originally lichen planus verrucosus. There is secondary lichenification which caused the different opinion as to diagnosis.

DR. OCHS: I treated this patient at Fordham Hospital last summer. He had typical lesions of lichen planus on the leg, and likewise on the chest. I think that it is a case of lichen planus verrucosus.

DR. GROSS: From the appearance of the patient's legs I would not be able to differentiate lichen planus from neurodermatitis verrucosa, but only two weeks ago the patient had typical patches of primary neurodermatitis on the arms which could not have been secondary to lichen, because there were no other lesions even suggesting lichen planus. The prompt response to treatment with tar is another point in favor of neurodermatitis. The great resemblance of some of the lesions to prurigo nodularis is an interesting feature, considering the difference of opinion as to the true nature of this disease.

DR. GOODMAN: It was my impression that on examination of the patient he evidenced a great deal of pleasure in presenting his lesions to the examining physicians. It occurs to me that not a small part of his skin trouble may have been self-induced. The linear arrangement along the front part of the lower legs suggested this. I advise that the limbs be dressed with an impervious dressing for several weeks.

ARSENICAL DERMATITIS. Presented by DR. CANNON.

J. R., aged 45, born in the United States, a porter, first came to the Vanderbilt Clinic in May, 1929, with an eruption on the penis and left forearm which had developed during antisyphilitic treatment. He had received ten injections of arsphenamine and four of mercury. During May, he underwent a course of treatment at the Vanderbilt Clinic. After one month's rest he began his second course on August 5. Immediately after the first injection (neoarsphenamine, 0.45 Gm.) his hands and feet became swollen and he noticed a spreading of the rash on the forearms. At that time there were papular lesions covered with shiny scales on the flexor surface of the forearms. Scaly eruptions were present on the elbows. There were some discrete papules on the neck and abdomen. Lesions of the same character were present on the feet. Lichen planus-like spots were seen on the buccal mucous membranes. An erythematous, exfoliating rash was present on the scalp and around the ears. There was hyperkeratosis of the palms, the hands were cyanotic and the lesions were pinkish blue. There was also a slight puffiness of the finger tips. The physical examination gave negative results, with the exception that the liver was enlarged.

The Wassermann reaction of the blood was 1 plus; the Kahn test, 0.4. A subsequent Wassermann reaction was 4 plus. The chemical analysis of the blood showed: sodium chloride, 487.6; sugar, 100.4; bile, 10.7; urea nitrogen, 11.6, and uric acid, 2.94. Since that time the patient had received twelve intravenous injections of sodium thiosulphate.

A biopsy showed marked keratosis. There were loose keratinized shreds on the surface. There was also some vesiculation. The superficial vessels contained fibrin and nuclear débris. The prickle cell layer showed a marked spongiosis and a marked infiltration with polymorphonuclears. There was also a marked acanthosis. The superficial corium showed a definite granulomatous infiltration whcih was superficial, but extended partly into the pars reticularis. The infiltrating cells consisted of plasma cells, endothelial leukocytes, many young fibroblasts, lymphocytes and polymorphonuclears. Deeper down in the corium there was also a perivascular infiltration of lymphocytes and plasma cells. Although the picture was not absolutely pathognomonic, it was consistent with the diagnosis of syphilis, particularly in view of the history. There were masses of chromatophores in the superficial corium, particularly in the papillae.

DISCUSSION

DR. MCCAFFERTY: In the case that I reported the patient had typical lesions of lichen planus on the skin as well as on the mucous membranes of the mouth and vulva. There were no hypertrophic lesions. She was a light mulatto. When the lesions of lichen planus began to disappear, a dark, slate-colored discoloration remained which lasted for almost a year. I believe that any one would have made a diagnosis of lichen planus in this case at that time because the lesions were so very typical.

DR. LEVIN: I recall the case that Dr. McCafferty reported. The clinical lesions were those of lichen planus. It is my opinion that arsenic has the power of stimulating the appearance of an eruption of lichen planus in persons who are predisposed to the condition. It may also produced an eruption that resembles lichen planus. We should distinguish between lichen planus in a syphilitic person and a lichen planus-like eruption from arsenic. It is also possible that arsenic may irritate the nervous system to produce lichen planus of the skin and mucous membranes.

DR. TRAUB: Was the diagnosis lichen planus and arsenical dermatitis, arsenical eruptions resembling lichen planus or syphilis? The skin lesions, in part, were those of arsenic poisoning, but many were quite typical lichen planus papules, showing the violaceous color, angulation, umbilication, etc., that are commonly seen. In addition, the lesions on the buccal mucosa and tongue, in particular, were characteristic of lichen planus. In a case such as this, which is representative of a group of cases of lichen planus appearing in a patient with arsenic poisoning, in which clinically and microscopically the lesions are indistinguishable from lichen planus, treatment does not help much in establishing a diagnosis because the course varies so much irrespective of therapy.

DR. FEIT: I do not agree with Dr. Levin and Dr. Traub. Although the lesions are clinically and histologically the same as lichen planus, they do not respond to treatment in the same manner. They clear up under treatment with sodium thiosulphate when caused by arsenic. The treatment alone could make the differential diagnosis.

DR. LEVIN: I believe that too much emphasis is placed on the value of sodium thiosulphate in the treatment for eruptions from arsenic and other metals. The impression that one gets when listening to discussions on its value is that it is specific in its action. I think that this is overestimated.

DR. CANNON: We had a number of patients in the Vanderbilt Clinic who developed lichen planus-like eruptions following the intravenous injection of one of the arsphenamines. The lesions are clinically and histologically indistinguishable from lichen planus found in people who have not received arsphenamine in any form. This has lead us to believe that lichen planus is a toxic manifestation and that arsenic is one of the chemicals capable of producing the disease. The lesions usually disappear following the cessation of arsenic, plus the administration of sodium thiosulphate. Usually these patients can continue treatment with arsphenamine without increasing the eruption.

DR. POLLITZER: Bearing on the interesting question of the etiology of lichen planus, during the World War statistics were gathered on the prevalence of lichen planus in England. It was shown rather definitely that during this very trying period in England there was no increase in the instance of lichen planus.

In regard to the occurrence of lichen planus after the administration of arsphenamine, about nineteen years after the introduction of arsphenamine and more than fifteen years after attention was called to the relatively frequent occurrence of lesions resembling lichen planus, subsequently shown to be identical in all respects with lichen planus following the administration of arsphenamine, it seems a little belated to discuss this matter. A lesion clinically resembling lichen planus in every respect and histologically identical with the papules of that disease does occur as a drug eruption after the administration of arsphenamine.

DR. ROSTENBERG: I am treating a patient now whom I showed at a previous meeting, who developed a lichen planus-like eruption on the hands during treatment with arsphenamine, which cleared up after cessation of treatment. The same eruption returned when a new course of treatment was resumed at a later date. To my mind, this proves that this eruption is a toxic phenomenon due to the arsenic, as it is not likely that a patient would have two attacks of lichen planus in a comparatively short time.

DR. TRAUB: Lesions which clinically cannot be differentiated from those those looked upon as characteristic of lichen planus on the mucous membrane are not produced in the usual picture of arsenic poisoning. In patients who have been or are being treated with arsenic and develop a lichen planus, lesions of lichen planus of the mucous membranes are possible, but to attribute these to arsenic requires an assumption that cannot be proved until the cause of lichen planus is known.

DR. SULZBERGER: As Dr. Pollitzer has just said, the question of the identity of the lichen planus-like arsenic eruption and real lichen planus has been discussed in the European literature for many years. Is the lichen planus-like eruption which we see after the administration of arsphenamine, and which is both clinically and histologically lichen planus as far as its morphology is concerned, a real lichen planus which has not been manifest, and which has laid dormant until the arsenic has caused it to appear, or is it a form of dermatitis medicamentosa caused by the eruption, and only morphologically, not etiologically, related to the disease known as lichen ruber planus Wilson?

I think that the majority today favor an affirmative answer to the latter question. The lichen ruber-like dermatitis caused by arsphenamine looks like lichen ruber planus because the body has at its disposal only a limited number of reaction types, and sometimes responds to various entirely different insults with the same morphologic tissue reaction. As an illustration of this, we all know that a histologically perfect tubercle is most frequently a tissue reaction to tubercle bacilli or their products, but are not necessarily always so. We can occasionally find tubercles in other conditions, which, according to our present knowledge, have no connection with the tubercle bacillus, such as actinomycosis, leprosy, kerion celsi, syphilis, and acne rosacea. It is not surprising, therefore, that just as other chronic inflammatory processes may simulate tuberculosis in their morphology, so the effects of arsphenamine can occasionally cause a picture identical with that caused by the harmful agent in lichen planus, or by the specific virus of herpes zoster.

DR. CANNON: As a rule, there is no evidence of arsphenamine dermatitis in patients who develop lichen planus after treatment with arsenic. Not infrequently, however, preceding the outbreak of lichen planus there is evidence of arsenical poisoning, such as swelling of the hands and feet, puffiness of the eyelids and redness of the palms and soles, as was indicated in this patient. In all such cases there is an accumulation of arsenic, as shown by tests of the blood and urine, corresponding with an appearance of the lichen planus. These eruptions of lichen planus have invariably disappeared following the administration of sodium thiosulphate and treatment directed toward the elimination of arsenic with no medication being given for the lichen planus.

DERMATOPHYTOSIS AND DERMATOPHYTIDE. Presented by DR. GROSS.

W. W. I., a negro, aged 29, was first seen at the Vanderbilt Clinic on the afternoon of presentation. The duration of the eruption was three weeks. According to the patient, it began on the hands. About a week after the eruption on the hands developed a generalized rash appeared on the body, starting in the groin and spreading rapidly to the trunk.

On examination, he showed a vesicular eruption of the palms with erythematous, scaly and macerated lesions in the webs and an extension of the eruption to the backs of the hands in the form of discrete and confluent papules. A few circum-

scribed, scaly patches were present between the toes, and the nails of both big toes were discolored, thickened and lifted up by a chalklike subungal mass. The outstanding feature was the condition of his body, which consisted of a generalized eruption of minute, lichenoid papules, partly discrete, partly confluent, from the neck to the thighs. Many of the confluent lesions were oval and were rather sharply defined and scaly, thus producing the picture of pityriasis rosea. Microscopic examination of the hand, toes, toe-nails and trunk gave negative results.

DISCUSSION

DR. WOLF: I agree with the diagnosis of dermatophytosis of the hands of the dyshidrotic type, but I hesitate to accept a diagnosis of lichen trichophyticus on the trunk. I am of the opinion that the eruption on the trunk is probably pityriasis rosea occurring in the course of acute dermatophytosis.

DR. GOODMAN: I was interested in the negative observations under the microscope for the lesions on both the hands and the feet. At the Skin and Cancer Hospital it is not unusual to find negative microscopic observations for tinea in lesions of the hands, although the lesions on the feet in the same patient are positive. Some time ago I had the intern on duty in the laboratory give me the figures, and I believe that the organisms were found thirty times in the examination of 100 feet and only three times in the lesions on the hands. Lesions of the hands simulating tinea and associated with tinea of the feet need not be due to the organism but may be a form of toxic eruption due to the toxin elaborated by the tinea organisms between the toes or on the soles.

DR. GROSS: I am afraid that it was premature to bring this patient before the section at this time. The microscopic observations from the different locations were negative at a last minute search. Cultures from the skin and blood cultures were taken. I am familiar with the work of Werner, Jadassohn and Peck in Zurich, as to the dermatophytide nature of eruptions on the hands, but I do not believe that we should generalize the theory. Primary dermatophytosis of the hand with convincing microscopic observations naturally exists. The resemblance of the eruption on the trunk to pityriasis rosea cannot be denied, but it is a strange coincidence that this should appear about two weeks after an acute vesicular eruption of the hands.

GENERALIZED ERYTHRODERMA. Presented by DR. HOPKINS.

S. R., a man, aged 39, an upholsterer, Polish, married, was first admitted to the Presbyterian Hospital on May 16, 1929, with a generalized eruption of two years' duration. It had begun when the patient was doing furniture painting, commencing on the hands and gradually spreading to the entire body. This cleared up somewhat with roentgen therapy, and then the patient developed a nasal obstruction which required operation; following this he developed numerous boils.

The patient received forty injections of sodium thiosulphate without improvement. From October 28 to April 29 he was treated at Unna's Clinic, and the skin almost cleared. Immediately on return to this country the lesions began to recur and the entire skin became involved, so that admission to the hospital was necessary. After two months in the hospital the skin almost cleared, only to recur in about a month, and the patient was readmitted on October 22.

Examination showed a chronic, generalized, exfoliating, macular and papular dermatitis. General examination was negative except for carious teeth and a palpable liver. The blood count was normal except for 15 per cent eosinophils. The skin tests were unsuccessful because of a generalized involvement of the skin.

Two biopsies were made. There was some hyperkeratosis and parakeratosis and moderate acanthosis. The stratum spinosum showed circumscribed edema and in some spots degeneration not warranted by the edema alone, as in precancerous conditions, but without dyskeratosis. Many dilated vessels were noted in the papillary body with elongated papillae and a moderate amount of edema. The blood

vessels of the cutis were also dilated and surrounded by plasma cells. (The large amount of plasma cells in the cutis was pathognomonic in other fatal cases of this type.) The basal layer and papillary body showed considerable pigment. An infiltration was present in the cutis around the sweat glands which in its polymorphism and cell degeneration reminded one of granuloma fungoides. The fatty layer showed infiltration of the cells. The histologic examination was not characteristic of any disease. Treatment consisted in strongly reducing remedies which showed the best results in diminishing the itching and clearing up the hard papules.

DISCUSSION

DR. WISE: The appearance of the skin gives the impression that later on the patient will develop a generalized atrophy and the condition will become pityriasis rubra of Hebra; eventually he will die of the disease.

DR. LAPOWSKI: I saw this patient two weeks ago in my office before he went to Dr. Hopkins. The whole body, from head to foot, presented lichen planus. In all such cases I watch for mycosis fungoides. No roentgen or ultraviolet treament should be given. It is important to follow such cases to the end and see the normal course of the disease.

DR. HOPKINS: This seems to be a peculiarly baffling case. The patient has had persistent erythroderma accompanied by severe pruritus with very unusual pigmentation. The appearance suggested one of the leukemia group in which I place mycosis fungoides. One thing that seems to help is isolation in the hospital. The patient quiets down and gets much better. I sent him to the country and he remained fairly well. As soon as he returned he became worse.

PREMYCOSIS FUNGOIDES. Presented by DR. MCCAFFERTY.

J. L. M., a man, aged 48, born in Hungary, a taxidriver, was admitted to the Vanderbilt Clinic on July 16, 1929, with an eruption that had been present for a year.

On examination, the patient showed an eruption arranged in plaques all over the trunk and extremities. The plaques varied in size from that of a quarter to that of a palm. The margins were indistinct and pinkish, with very fine scaling. There was very little infiltration. The palms and soles were free. Pruritus was present only at night. He had leukoplakia-like spots on the buccal mucosa.

Roentgen examination of the abdomen, urinalysis, blood count, chemical analysis of the blood, Wassermann test and arsenic and lead determinations gave negative or normal results.

Biopsy showed marked parakeratosis and edema of the prickle cell layer, and also acanthosis and marked infiltration of polymorphonuclears in the prickle cell layer. A few mitotic figures were seen. The corium just beneath the rete pegs was infiltrated with various types of cells. There were many lymphocytes and a few endothelial cells. Many newly formed blood vessels were seen, and an occasional plasma cell was noted. The papillae came quite close to the surface. The pathologic changes were consistent with the diagnosis of mycosis fungoides. That diagnosis, however, was not perfectly definite from the histologic standpoint.

The patient was treated with the roentgen rays on the right side of the body. Four fractional doses were given at weekly intervals. The right side improved; the left side did not.

DISCUSSION

DR. ELLER: I would be more inclined to a diagnosis of parapsoriasis in plaques because of the lack of itching and the appearance of the plaques.

DR. LEVIN: I agree with the diagnosis as presented. My first impression of the case was that of parapsoriasis in plaques. The lesions, however, were sharply demarcated, elevated and gyrate, and I think that a diagnosis of premycosis fungoides should be favored.

ENDOTHELIOMA (GENERALIZED). Presented by DR. WYETH.

C. Z., a man, aged 20, was presented before the section on Oct. 3, 1928. The eruption began on the chest at the age of 8 months and soon spread all over the body. It consisted of firm, bluish-red, shiny, smooth nodules, varying in size from that of a pea to that of a walnut. New lesions had continued to develop.

The patient's general condition had been good. There were no abnormal cardiorespiratory, gastro-intestinal or genito-urinary symptoms. The Wassermann reaction was negative on two occasions.

Paraffin section showed a cellular process which was closely associated with small capillaries and possibly arose from them. Some of the cells were pigment-bearing. There was no evidence of neurofibroma or epithelioma. The process was probably benign. The histology resembled most closely endothelioma of the skin (Ewing-Cutler).

On April 29, 1929, under ether narcosis, the tumors of the right leg were removed by surgical diathermy. The resulting wounds healed promptly. On June 20, under spinal anesthesia, the tumors of the left leg were removed in the same manner. The patient gained weight and at the time of presentation had returned to his daily occupation.

DISCUSSION

DR. ELLER: Last year we had a patient who had a nodule on the mucous membrane of the nose. This was removed. Dr. Ewing studied the tissue and made a diagnosis of endothelioma; he explained that the lesion was relatively benign and would not metastasize.

DR. OULMANN: This patient has certainly improved. The older members of the Manhattan Dermatological Society will remember a case reported by Dr. Dittrich, a hemangio-endothelioma congenitum. The second day after birth the infant developed tumors in the cutis which soon took on a bluish-red hue. They increased in size and numbers. The spleen was enlarged, and the infant died of marasmus when 6 weeks of age.

A CASE FOR DIAGNOSIS. Presented by DR. ANDREWS.

H. D., a white man, aged 56, a salesman, born in the United States, was admitted to the Vanderbilt Clinic on Oct. 28, 1929, with a lesion on the right suborbital region which had been present since birth. The patient said that it had increased in size just prior to presentation. Examination showed an indurated, wartlike lesion, the size of a pea on the right cheek, surrounded by a lunar-shaped ridge ending in a node. The lesion felt hard and was slightly excoriated. The impression gained was that the lesion was probably a mole, possibly a new growth, but was not of a serious nature.

DISCUSSION

DR. GROSS: I saw this patient about two weeks ago and made a diagnosis of squamous cell or mixed type of epithelioma. I think that the lesion has enlarged since.

MYOMA. Presented by DR. HOPKINS.

F. P., a white man, aged 56, English, was admitted to the Vanderbilt Clinic on July 5, 1929, because of tumors on the face, trunk and upper extremities.

The lesion on the face had been present since birth, and a short time later the lesion on the left arm appeared. There were no new lesions until four years prior to presentation, when lesions appeared on the trunk.

Examination showed numerous tumors, varying from 0.5 to 2 cm. in diameter, on the face and trunk. These tumors were bluish pink and some were soft and others hard. They were painful and tender on pressure. Clinically, the condition appeared to be a case of von Recklinghausen's disease. A biopsy was taken and showed a tumor made up of bundles of smooth muscle occupying the deep layers of the cutis.

DISCUSSION

DR. HOPKINS: I wish to present this case simply on account of its rarity. I think that at first sight we passed it over as something of little importance, until the pathologic report was returned which made it extremely interesting. I think that the section was absolutely convincing. The tumors are not like those of von Recklinghausen's disease; they suggest myomas belonging to the nevus group.

FIBROMA PENDULUM. Presented by DR. FEIT.

The patient, from the New York Skin and Cancer Hospital, was said to have had the condition since birth. There was a tumor mass consisting of baglike lesions, which varied in size from that of a hazelnut to that of a fist, consisting mostly of pendulous skin. The skin was of normal consistency; the surface showed sulci and gyri, in some places resembling the surface of the cerebellum. In some places the follicles were dilated and filled with comedones similar to the picture of rhinophyma.

The patient gave a history of having been operated on in 1910 at Mount Sinai Hospital, but had not remained there long enough to have the cure completed. Several scars were visible as a result of the operation.

BROMODERMA TREATED WITH SODIUM THIOSULPHATE. Presented by DR. FEIT.

The patient, from the New York Skin and Cancer Hospital, exhibited a typical nodular bromoderma. There was some improvement following three injections of sodium thiosulphate.

SCLERODERMA TREATED WITH SODIUM THIOSULPHATE. Presented by DR. FEIT.

The patient, from the New York Skin and Cancer Hospital, exhibited typical scleroderma of the face, chest, thighs, hands and feet, of two years' duration. There was a history of paroxysms of angiospasms of the hands and feet during which they turned white and were cold.

The Wassermann reaction was negative. There was a slight secondary anemia; otherwise, the blood count was normal. Laboratory examination showed: blood calcium, 10.1; carbon dioxide, 63.8 per cent, and phosphates, 4 per cent. The basal metabolic rate was reported as plus 16. Chemical analysis of the blood showed: sugar, 140, and chlorides, 437, on Sept. 18, 1929, and sugar, 121.8, and chlorides, 433.5, on September 30. The high sugar and low chloride metallic curve changed after the injections of sodium thiosulphate. After about sixty injections of this drug the patient noticed a softening of the hardened areas of skin. Arsenic was found in an abnormal amount in the urine.

EPIDERMOLYSIS BULLOSA. Presented by DR. MCCAFFERTY.

O. F., aged 2 years, from the Vanderbilt Clinic, since the age of 3 days had had numerous blisters all over the body, including the mucosa of the mouth. Healing of some of the blisters would be followed by an outbreak of others, usually on areas previously traumatized. The skin had never been clear. There was no history of a similar disease in the family. Examination of the blood showed: nonprotein nitrogen, 28 per cent; chlorides, 525; the blood plasma showed: nonprotein nitrogen, 22.2; chlorides, 575. Serum from a bulla showed: nonprotein nitrogen, 25; chlorides, 650. The blood count showed: hemoglobin, 76 per cent; red cells, 4,880,000; white cells, 20,400; polymorphonuclears, 49 per cent; lymphocytes, 50 per cent; eosinophils, 1 per cent. The skin permeability to albumin was reported as 93 per cent.

The patient was treated for two weeks with injections of pituitary extract with no improvement, and was then given seven intramuscular injections of whole blood

from the mother with no improvement. At the time of presentation, the patient was being treated with small doses of ultraviolet light every two days.

A CASE FOR DIAGNOSIS. Presented by DR. MCCAFFERTY.

J. F., aged 26, was admitted to the Vanderbilt Clinic on March 1, 1929, because of dermatitis venenata. He was a photographer and handled chemicals. In November, 1928, he had noticed the appearance of papular lesions, varying in size from that of a pinhead to that of a split pea, on the forehead. This eruption soon spread over the body to form large scaly patches. The condition was diagnosed as eczema, and he received several roentgen treatments without improvement. In July, 1929, the condition cleared up complete following a three weeks' vacation in the mountains. He had a recurrence shortly after he returned to work.

At that time patch tests were positive for metol, bichromate, oxalic acid and bromides. In April, 1929, while in Florida, the dermatitis cleared up again, to return two weeks later when the patient returned to work. More recently, the condition had been very resistant to all forms of treatment and had not improved despite the fact that the patient was not exposed to chemicals.

Examination showed a brownish to slightly purplish nodular eruption scattered over the face. Some of the nodules were discrete, and some were confluent, forming small patches. The nose was covered with thick scales. There was partial loss of the eyebrows. Scattered over the trunk and lower extremities were variously sized, sharply defined, purplish-red patches. Some of these patches were crusted, some were ulcerated and some were surmounted by rather firm scales. Some of the areas suggested atrophy. There was a generalized edenopathy.

Biopsy taken one month prior to presentation showed marked hyperkeratosis, slight parakeratosis and superficial vesicle formation. The granular layer was pronounced in most places. The prickle cell layer showed edema, spongiosis and a marked acanthosis with occasional mitotic figures. Some slight infiltration, in places with polymorphonuclears, was observed. There were edema of the corium, many chromatophores, many newly formed blood vessels and a marked granulomatous perivascular infiltration particularly at the junction of the papillary and the reticular layers. These infiltrating cells consisted of fibroblasts, plasma cells, polymorphonuclears and lymphocytes. The histologic diagnosis was chronic vesicular squamous dermatitis.

The Wassermann and Kahn tests of the blood gave negative results. The blood count was normal. On Oct. 17, 1929, the chemical analysis of the blood showed: sodium chloride, 454.3; sugar, 117.7; bile, 9.61; urea, 14.05; uric acid, 3.45.

MONILETHRIX. Presented by DR. ANDREWS.

E. P., a white school girl, aged 14, born in the United States, was admitted to the Vanderbilt Clinic on Oct. 18, 1929, with a condition of the scalp that had been present since early childhood. No other members of the family had been similarly affected.

Examination of the entire scalp showed a dry scaling and the hairs were sparse and stubby, being broken off. They could be pulled out easily and were brittle. When examined microscopically with a low power objective or even with the naked eye, the hairs were seen to consist of fusiform swellings between which were constrictions. There was keratosis pilaris of the back of the neck and of the temporal regions. The hairs on the other parts of the body were not affected.

The basal metabolic rate was reported as plus 15.

A section showed a moderate hyperkeratosis, but otherwise there were no remarkable changes. Some of the hair follicles contained fairly well developed hairs; other contained a keratin-like material that was somewhat basophilic. The hair was very narrow. No diagnosis could be made on a histologic basis, but there was a suggestion of a definite dystrophy of the hairs from their appearance in the follicles.

NEUROFIBROMA. Presented by DR. CANNON.

W. H., a white man, aged 63, single, an American, was admitted to the Vanderbilt Clinic five months prior to presentation. He said that about fifteen years previously he had noted two lumps on the right forearm. The lesions had continued to grow slowly. About the same time a few small tumors began to appear on the trunk. They increased slightly in size and greatly in number during this time, localizing almost entirely on the trunk. There were no symptoms except slight tenderness where the tumors occurred at pressure points.

The trunk, especially toward the midline posteriorly, was covered with several hundred tumors. They were all shapes and sizes up to 2 cm. in diameter, discrete and in clusters, faun to deep brown in color. All of the lesions were soft and occasionally were herniated. In addition to this, there were a few pigmented macules and small brown papules. Similar tumors were scattered over the face, upper arms and scrotum. On the right forearm there were two subcutaneous tumors about 5 cm. in diameter, which were soft, nontender and definitely encapsulated. The skin over these areas was entirely normal.

General examination showed a lack of body hair over the pubis, bilateral inguinal hernia, well developed mammary glands, hypospadia, arteriosclerosis and chronic nephritis.

Neurologic examination was negative except for retinitis with multiple hemorrhages and exudate (probably cardiorenal).

Roentgen examination of the skull and long bones was negative except for marked thickening of the tables of the skull especially in the region of the occiput.

On May 20, 1929, a biopsy of the herniated tumor, stained with silver stain, showed: The skin was surmounted by two small nodules one of which was attached to the skin by a narrow pedicle. These nodules were covered by stratified squamous epithelium which contained a considerable amount of brown pigment in the basal layer of cells. There was a little pigment in the skin beneath the nodule but not nearly as much as in the nodule itself. The nodule was composed of delicate interlacing strands of nerve fibrils and collagen. The nerve fibrils appeared as hollow tubes best seen in a cross-section. Occasionally a small amount of pink-staining material was seen in one of the tubes. This was apparently the myelin sheath.

On September 25, a biopsy of a pedunculated tumor was made (hematoxylin and eosin stain): A section of a tumor removed from the skin showed a rather atrophic epithelium and a deeply pigmented basal cell layer. The superficial corium was arranged more or less parallel with the surface. Deeper down many small blood vessels were seen. There was a reticulated appearance in places; in others, fibers were more or less parallel and long. The tissue was very cellular. The nuclei were spindle-shaped and deeply staining. The section had definitely the appearance of a fibroma or neurofibroma. Trichrome staining showed definite nerve fibers. Definite nerve bundles were also seen in the hematoxylin and eosin sections. A silver impregnation stain showed a definite, fine, fibrillar appearance with fibers running more or less parallel in places and suggesting nerve fibers.

MAX SCHEER, M.D., *Secretary*

Regular Meeting. December, 1929

JOHN FRANK FRASER, M.D., *Chairman*

AINHUM. Presented by DR. GROSS.

J. R., a negro, aged 39, married, born in the British West Indies and a resident in the U. S. for eight years, gave a history of injury to the little toe about one year prior to presentation. Shortly after that he noticed a constriction at the

base of the same toe, which gradually became worse. There had been considerable pain. The left little toe soon became affected and showed the same development as the right.

Examination revealed no disturbance of the nervous reflexes. On the fifth toe of both feet were bands of constriction situated at the base of the toe. The constricting band on the left toe was less advanced than that on the right. The latter was constricted to about one-fourth the thickness of the toe. Distal to this was a swelling so that the end phalanx had become but a blunt, fleshy mass. The nail was completely gone.

DISCUSSION

DR. ANDREWS: I think that microscopic examination of the toe-nails would prove interesting as they show definite malformation which suggests the possibility of a fungus infection.

DR. POLLITZER: There is little to discuss in this case. I think it is remarkable that a man who has been away from the tropics where ainhum is not uncommon and who has lived in New York for at least eight years should begin to show signs of this extraordinary condition within the last year or two. In that respect the case is worthy of note.

DR. GROSS: This is the third case of ainhum observed at the Hospital for Joint Diseases in the past two years. The history of trauma is interesting in this case; it may suggest the theory of a trophoneurosis. I shall take scrapings from the toe-nails, but believe that they show only trophic changes.

LUPUS ERYTHEMATOSUS DISSEMINATUS. Presented by DR. WALZER for DR. LAPOWSKI.

S. H., a boy, aged 6½ years, had one sister who was said to have had tuberculosis. The Pirquet test and a roentgen examination of the chest were reported to give negative results. The tonsils had been removed at the age of 3. When about 8 months of age he had had a cervical gland removed.

The eruption dated back about three years and had begun on the face as two red, annular spots which had gradually spread. About six months later the eruption spread to the neck, chest and hands. The lesions on the back, the chest and the lumbar region, according to the mother's statement, had developed about five or six months prior to presentation, following treatments with ultraviolet light.

When presented the entire face was one erythematous patch, not infiltrated but covered with a fine furfuraceous scale. No atrophy was visible, and the erythema disappeared under pressure. The neck and chest showed similar erythema, not elevated or infiltrated, but covered with a fine furfuraceous scale. The back showed one large, irregularly shaped, erythematous patch with various shades of red and brown. The lower part of this erythematous patch was a darker red and was covered with a fine furfuraceous scale, but also intermingled with light brown pigmented spots, remnants of past lesions. The mucous membranes showed no lesions.

DISCUSSION

DR. FEIT: I agree with the diagnosis of lupus erythematosus, probably caused by exposure to the light. I have seen several cases of this kind. Give the patient resorcin internally. We have been under the impression that resorcin has been a desensitizer to light. The lesions clear up much more rapidly, and it would be worth while in all cases that are light-sensitized to try this treatment.

DR. TULIPAN: I should like to know if an examination was made for hematoporphyrin.

DR. CHARGIN: This patient was in Mount Sinai Hospital about two years before presentation. At that time he suffered from some general disturbance, the nature of which I do not recall. Because he presented an eruption on the face the dermatologic department was requested to see him. The eruption, which

was limited to the anterior aspect of the face, was strikingly like sunburn. In tracing the history is was ascertained that the patient had been purposely exposed to the direct rays of the sun for, as I recall it, cervical adenitis. He has had an acute burn of the face which has persisted. Although considered we hesitated at first to make the diagnosis of lupus erythematosus because of the rarity of this condition in children. As time progressed, however, we were forced to consider this as the most likely diagnosis, and he was presented before the Mount Sinai Dermatological Clinical conference with this diagnosis with which everyone present concurred. As viewed now, we must still regard this case as lupus erythematosus.

DR. WISE: I accept the diagnosis as presented.

DR. ABRAMOWITZ: I think that the lesions conform more to lupus erythematosus than to any other disease of the skin. The lesions are on the exposed parts of the body, a common occurrence in the disseminated types of lupus erythematosus.

DR. WALZER: This is not a case of light sensitiveness. The patient happened to get the lesions on the exposed parts. No examination was made for hematoporphyrin. The patient is tuberculous, and while the rash is not exactly typical of lupus erythematosus and no atrophy can be noted, the distribution, peculiar arrangement, sharp demarcation and the persistency of the lesions would point to no other diagnosis. On the other hand, lupus erythematosus disseminatus is extremely rare in children, although a number of cases have been reported.

LYMPHOGRANULOMATOSIS INGUINALIS (NICOLAS-FAVRE). Presented by DR. GROSS.

J. S., a negro, aged 27, single, born in Maryland, was admitted to the Presbyterian Hospital on Nov. 19, 1929. He gave a history of a penile lesion occurring eight weeks previously. About two weeks later he consulted a physician on account of the swelling of the inguinal lymph glands. The glands were incised and pus was found. About a week later another incision had to be made. Shortly before admission the patient felt sick, had chills and headache and had pains in his joints. On examination, a hard scar, the size of a lentil, was found on the dorsum of the penis. In both groins there were masses of swollen lymph glands which could be felt below Poupart's ligament. There were several incised glands, some of which were discharging a slight amount of thin pus. There was some reddening of the skin in this region.

The Wassermann reaction of the blood was negative; blood culture and culture from the pus were also negative. The blood count showed: hemoglobin, 92 per cent; red cells, 4,310,000; white cells, 15,100; polymorphonuclears, 74 per cent; lymphocytes, 20 per cent; large mononuclears, 3 per cent, and eosinophils, 3 per cent. The patient showed some marks from an eruption which had developed after he had taken "SSS" (iodide eruption).

DISCUSSION

DR. WISE: In connection with this case it is interesting to note that Pardo-Castello of Havana read a paper before the American Dermatological Association on lymphogranulomatosis inguinalis several years ago. The discussion of his paper indicated that a good many of those present did not know what he was talking about. Since the publication of Pardo-Castello's article, a book has come out by Hellestrom of Stockholm, in which he deals with the subject quite comprehensively. At the time that Pardo-Castello read his paper there was confusion in the minds of his audience as to the differentiation between lymphogranulomatosis inguinalis and granuloma inguinale. Lymphogranulomatosis inguinalis occurs in the glands of the groin, and the antecedent penile lesion is frequently overlooked by the patient as well as the physician. Granuloma inguinale has its initial lesion in the skin, in which the causative organism may often be demonstrated, whereas in lymphogranulomatosis inguinalis no amount of investigation has been

successful in demonstrating any causative organisms in the affected inguinal glands or elsewhere.

DR. THORNLEY: In the past five or six years I have seen many cases among sailors that resembled this case very closely, except that often enough we were unable to find any evidence or history of a lesion on the penis or anywhere else. Some of our cases go to suppuration, and after suppuration occurs they have exactly the same appearance as this case.

The frequency of these cases in sailors from tropical countries, where it is customary to go barefoot, would justify the suspicion that the causative organism might gain entrance through cracks in the skin of the feet without setting up any noticeable lesion at that site.

DR. CANNON: My patients are usually cured by exercising cleanliness, sterilization of the initial lesion and irrigation of the suppurating glands with potassium permanganate. I have given potassium iodide with good effect.

DR. SULZBERGER: As far as the clinical picture is concerned, I believe that there can be no doubt that this is a case of lymphogranulomatosis inguinalis. It corresponds to a number of cases that I have seen in Breslau, as I happened to be fortunate enough to be there about the time they were first observed in central Europe. This disease must be kept distinct in our minds from granuloma inguinale. The differences were well brought out in articles that appeared in the ARCHIVES in 1926, by Pardo-Castello, and in 1928, by Hillsman and his associates. There is one way in which we can be more certain of the diagnosis of lymphogranulomatosis inguinalis; that is, to test the cases with vaccines that are prepared according to Frie's method, from pus gained from an unopened bubo of lymphogranulomatosis inguinalis. This vaccine is injected intradermally into the patient whose case is being investigated. A positive reaction appearing forty-eight hours later designates that the case is one of lymphogranulomatosis inguinalis.

Until now, reports concerning the verification of this reaction of Frei have been to the effect that it is apparently specific. I suggest that this test be made in the case presented in order to establish the certainty of the diagnosis.

It is further interesting to note that cases of esthiomene and of syphiloma anorectale were also found to be positive to injections of Frei's vaccine, and for this reason they are now regarded by many to be forms of lymphogranulomatosis inguinalis.

DR. CANNON: I have shown several cases of lymphogranulomatosis inguinalis before the Section, one a little more than a year ago in a white man with a penile lesion followed by a bilateral inguinal adenopathy. We have seen about fifteen cases in the City Hospital and in no instance have we been able to isolate the specific organism. We have inoculated the pus into animals with negative results. We have also taken the sterile pus and injected it subcutaneously, which produced a large local reaction and in some instances a focal and constitutional reaction. We considered the Frei test of considerable importance.

DR. HOPKINS: I think with Dr. Cannon and Dr. Thornley, that this condition is probably more common than is recognized, and I am glad that Dr. Gross has again called it to our attention. I presented a case before this Section in 1926, and at the Vanderbilt Clinic we have since seen a number of others which seemed to belong to this category. Most of the patients have been negroes. I suspect that in the large negro population of this city the disease is no great rarity.

DR. GROSS: I cannot agree with Dr. Sulzberger about the first European observations. The condition was seen in Europe for many years and was given different names, but only after the publications of Durand, Nicolas and Favre was it recognized more generally as a clinical entity. This was also due to its apparent propagation during and after the World war.

We intend to excise one of the glands to prepare a Frei antigen and test the patient with it. The positive Frei test in esthiomene is interesting, but I can conceive only a certain percentage of cases to be due to an old infection with the virus of lymphogranuloma inguinalis. A few weeks ago we had a patient at

the Presbyterian Hospital with esthiomene or rather so-called syphiloma anorectale (Fournier) without scars in the inguinal region or any history of swollen lymph glands in the past. As far as the treatment is concerned, I did not find it as simple and successful as Dr. Cannon. I had a good result in a case of long standing several years ago by the use of filtered roentgen rays.

SYPHILITIC ULCERATION OF THE NOSE. Presented by DR. COMBES.

B. C., a negress, aged 48, said that two years prior to presentation she had developed a sore on the mucous membrane of the left nostril which had since increased in size, destroying part of the nose. During a period of four years, her weight had dropped from 200 to 112 pounds (from 90.7 to 50.8 Kg.). A brother died of pulmonary tuberculosis. She had had about twelve injections of arsphenamine and six of bismuth, with some local improvement and more pronounced general improvement.

On examination she presented an extensive ulceration of the cartilaginous portion of the nasal septum, but no involvement of the adjacent skin or of the other cartilages. The surface was smooth and clean. There was no involvement of other mucous membranes. She had a superficial soft ulcer, about 1 by 2 cm., on the left eyelid of two months' duration. There was distinct cavernous breathing below the right clavicle. The Wassermann reaction was reported as positive. Smears for acid-fast bacilli from the ulcerations were negative.

DISCUSSION

DR. SAUNDERS: In view of the fact that there has been very little response in these lesions to treatment and as the lesion on the inner canthus of the left eye has developed under treatment, I would like to suggest a diagnosis of tuberculosis. I understand that the patient also has tuberculosis of the lungs.

DR. GROSS: I would like to mention the possibility of mycosis fungoides.

DR. HIGHMAN: I think that the lesion at the canthus of the inner left upper eyelid should be considered in the discussion. I do not think that it is syphilitic. Epithelioma should be ruled out.

DR. WISE: The lesion on the eyelid and the destructive lesion on the nose are probably syphilitic, but neither are characteristic of syphilis. I think that the case deserves discussion from another aspect; for example, the nasal lesion resembles that of gangosa.

DR. COMBES: The case was presented more for discussion than for definite diagnosis, although a diagnosis of syphilitic ulceration was made. We considered tuberculosis, but a definite diagnosis of tuberculosis was not made because we had nothing to substantiate it, except the fact that the patient had tuberculosis of the lungs.

She has not improved very much under treatment. The treatment administered was not given by us, but was the intravenous injection of some preparation, probably arsphenamine. Of course, many of the late lesions of syphilis do not respond quickly to arsphenamine. We shall attempt to make a definite diagnosis with guinea-pig inoculation.

PSORIASIS AND LICHEN PLANUS. Presented by DR. BLOOM.

J. O., a man, aged 60, came to the clinic in 1923, with a dry, scaly, papular eruption of many years' duration, located on the extensor surfaces of the forearms, legs and scalp. This condition was diagnosed as psoriasis and was treated thereafter only with ointments. Arsenic was never administered to the patient. The eruption disappeared and recurred from time to time.

On Nov. 9, 1929, the patient returned to the clinic presenting the old psoriatic eruption which was, however, associated with a typical eruption of lichen planus of one week's duration.

The psoriatic eruption consisted of a moderate number of erythematous, dry, scaly, slightly infiltrated papules, varying in size from that of a pinhead to that of a dime, on and below both elbows. A little below the right knee there was a sharply defined, similar lesion, the size of a nickel. When the white scales were rubbed off with the finger-nail, bleeding points were seen. The eruption did not itch and had been present with some interruption for fifteen years.

On each buttock near the intergluteal fold there was an irregular, somewhat bluish, scaly, flat lesion, the size of a half dollar, which did not look like a psoriatic lesion and in which bleeding points were not seen on scratching. The duration of the lesions was unknown to the patient.

The typical pruritic eruption of lichen planus consisted of numerous violaceous papules, varying in size from that of a pinhead to that of a dime, some of which were distinctly umbilicated. The lesions were seen on the dorsal surface of the feet, on the glans, corona and shaft of the penis and on the scrotum. The mucous membranes of both cheeks showed bluish-white lesions, the size of a pinhead and larger, some arranged in ring and net form.

Histologic examination confirmed the clinical diagnosis of psoriasis and lichen planus.

DISCUSSION

DR. CANNON: Lichen planus and psoriasis are occasionally difficult to distinguish from each other. A number of years ago in association with Dr. Fordyce, I saw a case that illustrates this particular point. Early every summer when the patient was on her way to Maine we would make a diagnosis of psoriasis and on her way south in the fall, it was usually changed to lichen planus. Still another instance was seen in a patient referred to Dr. Fordyce by a prominent dermatologist for an opinion as to whether the patient had lichen planus or psoriasis, the physician having made each diagnosis, from time to time, on several occasions. I think that we have all seen similar cases and that ultimately these patients are usually thought to have lichen planus rather than psoriasis.

DR. POLLITZER: The discussion about lichen planus and psoriasis suggests to me that Hutchinson, fully fifty years ago, described what he called, with his fondness for compound names, lichen psoriaticus. I imagine that the case presented comes in that category. There is no doubt as to the lichen planus, and it is not an unusual observation in lichen planus to have patches that suggest psoriasis.

DR. ROSTENBERG: I have seen a case of combined psoriasis and lichen planus, the psoriasis being of long standing. The patient developed the lichen planus after she had received arsenical treatment for a long time. I then thought that the lichen planus was a toxic rash sometimes seen after the use of arsphenamine.

DR. WISE: I had the opportunity of seeing this patient one month ago when the skin had not been subjected to as much treatment as it has been since. At that time both types of lesions were characteristic. There was psoriasis of the elbows and lichen planus of the back of the hands, both types of lesions being unmistakable clinically.

DR. HIGHMAN: This case merits a little more discussion. Most of the lesions are lichen planus. The lesions that remind one of psoriasis are chiefly those on the patella and extensor surfaces of the elbows, and there the skin is rather thin and puckered. Of course, lichen papules when fused have a psoriasiform appearance and these may be of that sort. Therefore, it seems to me that a further histologic study should be made of both types of lesions as a control against each other and in order to make sure that this is a mixture of these two common diseases.

DR. HIGHMAN: It seems significant to me against psoriasis that the patient's scalp is free. If the patient had had psoriasis for fifteen years, some lesions should be in the scalp.

I do not think that we can ever say that the lesions are one thing or another. I know that they can look very much alike; nevertheless, we have to go a little bit further to be sure, and I would invoke the microscope for definite diagnosis.

There is no doubt that the patient has lichen planus, but whether he has lichen planus with psoriasis is a question. I have seen cases of lichen planus recur over and over again over a period of from eight to ten years.

DR. BLOOM: There is no doubt in my mind that the diagnosis is correct as presented, as I have seen this patient frequently with his psoriatic eruption on the elbows and knees, and I saw him with his recent typical eruption of lichen planus on the back of the hands and feet, on the genitals and on the mucous membranes of the mouth. In his history chart for 1927, I found that lesions were then present on the scalp.

As the association of psoriasis and lichen planus seems to be rare, and to my knowledge not mentioned in the literature, I thought it advisable for the record's sake to remove a papule from the patient's elbow and one from the dorsum of the hand for histologic examination. The microscope confirmed my diagnosis. The papule from the elbow shows the picture of psoriasis; that from the dorsum of the hand, lichen planus.

A CASE FOR DIAGNOSIS. Presented by DR. WALZER for DR. LAPOWSKI.

F. S., a woman, aged 29, married, had had five children and had never been sick. She said that she had not taken any internal medicine for a number of years. She also said that the condition began with a generalized itching and dermographism. The discoloration of the skin came on later. About the same time as the pruritus of the body occurred, numbness of the fingers developed which had been progressive in that the patient had recurrent attacks in the fingers, white then blue, then red, on exposure to cold. The patient complained that the fingers at that time were very stiff. About ten months before presentation she had had ulcerations at the tips of the index, middle and fourth fingers of the right hand. She showed the following conditions on presentation: The entire skin from the face down was of a muddy discoloration, in some locations more pronounced than in others, and in other locations, i. e., on the back, neck and legs, the skin presented a peculiar mottled appearance. The mottling was produced because the follicular openings were pigmented, compared with immediately surrounding skin, which was leukodermic, and the dark pigmented skin to the outside.

The outer part of both arms showed distinct subcutaneous indurations which could be felt in nodules and in larger plaques. The left third, fourth and index fingers showed scars at the tip, the result of previous ulcerations. Dermographism was fairly pronounced.

DISCUSSION

DR. GROSS: Has a basal metabolism determination been done in this case?

DR. WALZER: It has not been done.

DR. CHARGIN: I think that we are dealing with scleroderma. The pigmentation, the somewhat indurated feel of the skin and the sclerodactylia all speak in favor of scleroderma as the most likely diagnosis.

DR. ANDREWS: I agree with Dr. Chargin, and I think that it is a typical case of scleroderma. I could not feel the subcutaneous nodules mentioned in the history.

DR. POLLITZER: This case impresses me as a somewhat unusual type of scleroderma. It has atrophies that are dotted over large areas, instead of being in one or more large sheets. There is a punctate atrophy of the skin, and there are the pigmentations common in scleroderma. It presents, furthermore, a good example of sclerodactylia, which is simply a local form of scleroderma. I should say that it is definitely a case of endocrine dysfunction with symptoms of scleroderma.

DR. WISE: I agree with Dr. Pollitzer.

DR. HIGHMAN: The possibility of scleroderma is to be considered, but a good many other things are to be suggested. I would rather await future developments of the case.

DR. WALZER: This case was shown mainly for a clinical diagnosis. There are two possible suggestions for diagnosis. One is Raynaud's disease which, however, would not account for the pigmentation; the other, an early case of scleroderma, which would probably account for all symptoms. There has been some interesting work done recently along this line. Thomas Lewis of England has shown that Raynaud's disease is neither a nervous phenomenon nor a capillary disease. He has proved experimentally that the condition is due to hypersensitiveness of the digital arteries, in that they react abnormally to cold, producing the Raynaud syndrome. In conjunction, Lewis said that many of those conditions that simulate Raynaud's disease (and he especially mentioned sclerodactylia) will eventually be proved to be of a similar process, and in this way Raynaud's disease may be closely connected with scleroderma.

Some interesting work has been done on scleroderma by Longcope of Johns Hopkins. One thing is common in all cases of scleroderma, i. e., they have sclerodermic tissue, but they also have other symptoms that may vary with every case, symptoms referable to involvement of the internal organs, the endocrine glands, etc., showing abnormal sensations, Raynaud's syndrome and symptoms associated with the involvement of the endocrine gland.

In a case of scleroderma in which the patient died with symptoms of Addison's disease, sclerodermic changes were demonstrated in the suprarenal glands and the testes. Addison believes that scleroderma is primarily a local condition of the skin with secondary sclerodermic involvement of the internal organs or glands. The symptoms of thyroid deficiency are seen occasionally in sclerodermic patients and are not the primary, but the secondary, cause of the disease. In other words, scleroderma is an infiltration of the skin with secondary involvement of the internal organs.

This case coincides with the recent reports mentioned. The condition began with pruritus and pain in the tips of the fingers. The patient developed pigmentation later, and finally infiltration occurred. I think that the condition is scleroderma, with some suprarenal changes and Raynaud's syndrome.

PRURIGO NODULARIS. Presented by DR. WALZER for DR. LAPOWSKI.

B. R., a woman, aged 43, married, with two children, had never been sick. She had never had any previous eruption. The condition for which she was presented dated back about three and a half years, and had begun with itching on both legs, followed later by lesions.

On examination, the lower extremities, from the knee down, especially the left, showed many scattered, infiltrated, elevated, dark red nodules, varying in size from that of a pea to that of a dime, with round tops and surrounded by dry, adherent scales, almost verrucous-like. In the center of the left leg was a brown, darkly outlined scar, the size of a dime, which the patient said was due to a similar lesion that had become infected.

NEW YORK DERMATOLOGICAL SOCIETY

J. FRANK FRASER, M.D., *Secretary*

Regular Meeting, Nov. 26, 1929

PAUL E. BECHET, M.D., *President*

A CASE FOR DIAGNOSIS. Presented by DR. FRASER.

A young woman, from the Cornell Clinic, presented ulcerating lesions on the legs, arms and forearms, some of which had healed spontaneously, leaving keloidal scars. The duration of the condition was sixteen months. There was no history

of taking drugs, and the patient said that there had been no injury. Wassermann tests had been made before the patient came to the clinic and were negative. The psychiatric department reported that there were no mental or behavior disorders and nothing to suggest that the condition was a dermatitis factitia. The patient had had one injection of arsphenamine and one of bismuth. The possibility of tuberculosis cutis had been considered. Biopsy was refused.

DISCUSSION

DR. MALONEY: I am more in favor of the diagnosis of dermatitis factitia than of tuberculosis cutis.

DR. WHITEHOUSE: I am in favor of the diagnosis of blastomycosis. I think that that is more logical than bromide eruption or the other suggestions.

DR. KINGSBURY: I think that the fact that some of the lesions have healed and that they are in different stages of development is against the diagnosis of blastomycosis. My clinical diagnosis would be bromoderma, but there is much to suggest a possible dermatitis factitia.

DR. HOWARD FOX: Dr. Fraser said that a biopsy had been refused. All that is needed to prove the presence of the organism of blastomycosis or coccidioidal granuloma is a culture, which can be made from the pus without disturbing the patient.

DR. WISE: I saw several cases in San Francisco which bore a resemblance to these active lesions and to the scarring. I suggest the diagnosis of granuloma coccidioides.

A CASE FOR DIAGNOSIS (ERYTHEMA ELEVATUM DIUTINUM?). Presented by DR. MACKEE.

J. F., a man, aged 29, an actor, from the New York Post-Graduate Clinic, gave a history of tuberculosis in several members of the family, although he had never had clinical tuberculosis. There was no history of rheumatism, although there was some difficulty with one shoulder which was said to be a congenital deformity. The patient had had hay-fever, and there was a history of this disease in the family.

There was a single lesion on the knuckle of the right middle finger, of one year's duration. The lesion consisted of a firm, movable, dry, rather poorly outlined, round nodule, 1 cm. in diameter, elevated about 2 or 3 mm., very slightly erythematous, with a suggestion of a verrucous surface. There were no subjective symptoms. Very slight improvement followed six fractional, unfiltered roentgen treatments.

The diseases that had been considered were tuberculosis verrucosa cutis and erythema elevatum diutinum.

NOTE.—Subsequent bacteriologic and mycologic examinations gave negative results. After cauterization, all attempts to demonstrate bacteria from within the lesion and cultures and several inoculations were negative. Attempts to obtain fungi before cauterization gave negative results. Microscopic examination of the lesion revealed nothing but inflammation of the type seen in lichenified eczema. There was no degeneration and no conspicuous change in the connective tissue or walls of the vessels.

DISCUSSION

DR. BURNETT: I favor the diagnosis of tuberculosis verrucosa cutis. The surface has apparently been smoothed as the result of roentgen treatment.

DR. MALONEY: I incline to the diagnosis of erythema elevatum diutinum. It much resembles the case published by Dr. Trimble, the only difference being that there were two lesions in his case and the color in this is different; the lesion is of a decidedly dusky color, whereas in Dr. Trimble's case it was a much brighter red. I think that that is the correct diagnosis.

DR. WISE: I agree with Dr. Maloney that the condition is erythema elevatum diutinum.

A CASE FOR DIAGNOSIS (DERMATITIS ARTEFACTA?). Presented by DR. TRAUB.

M. U., aged 24, a stenographer, born in Virginia, presented an eruption which began when she was 4 days old, and which had persisted ever since with the exception of the summer time, when it practically disappeared. The nose was always sore. The patient said that she had not used anything on the lesions except cold cream. She could not tell how the spots began as she did not notice them until they were large scaly areas. She had never noticed blebs. Twelve or thirteen years before presentation, she had a different sort of eruption which confined her to bed for about a month; this eruption was characterized by large crusts (the size of a quarter) with pus under them.

The entire skin of the hand peeled off about ten years previous to presentation, since which time there was an occasional mild degree of peeling of the fingers. The itching was rather marked, particularly when the patient was overheated.

DISCUSSION

DR. MACKEE: The linear lesion in front of the left shoulder and the fact that the eruption is sharply grouped and marginated suggest the possibility of dermatitis factitia but, of course, if the history is correct, that diagnosis is impossible; also, it looks like the remnants of a bullous impetigo, but the history negatives this diagnosis also. The case does not correspond with our conception of epidermolysis bullosa hereditaria. I suspect that long study of the case will be necessary before a diagnosis is established.

DR. RULISON: I think that it is a self-induced eruption and that the patient is not giving a true history of either the duration or the course of the lesions. I venture to suggest that it is done with the stopper of a bottle, with which she touches the skin.

DR. HOWARD FOX: I do not see how this condition can be considered a case of self-inflicted eruption. In the first place, it is fairly symmetrical; as a rule, this is not true of self-inflicted eruptions. In the second place, the lesions are certainly not within easy reach of either the right or the left hand; it would be awkward indeed for the patient to produce some of the lesions in the scapular region. Again, the patches did not have unnatural appearance or angular border, though one of them was linear; there were no tabs or downward prolongations which might have followed the use of a chemical caustic. If the history of life-long duration of the disease is correct, a diagnosis of self-inflicted eruption could not be considered. While unable to make a diagnosis, I would suggest that Dr. Traub make a histologic examination and stain for elastic fibers, which are often absent in cases of epidermolysis bullosa.

DR. WISE: I agree with Dr. Fox that the eruption is not an artificial dermatitis. The lesions represent an instance of hypersusceptibility to the staphylococcus and streptococcus organisms normally existing on the patient's skin.

DR. WHITEHOUSE: I do not think that the eruption is dermatitis factitia; the history is rather against that. She told me that the least knock brings them out. She had two on the extensor surface of one finger — two recent ones — and the lesions evidently had a ring around them, like a flattened bulla. The lesions on the shoulder and arm have a fringe such as one gets from bullous impetigo contagiosa. I am wondering if epidermolysis bullosa might not be considered. Dr. Fox spoke of elastic tissue. I did not see any miliary cysts, but wondered if any one thought of that possible diagnosis; the long duration and strange behavior would suggest it.

DR. MACKEE: The patient said that the lesions might occasionally occur as the result of traumatism, but that most of them were spontaneous; also, the presenter was unable to produce lesions by rubbing the skin. Finally, there is no atrophy and there are no cysts on the backs of the fingers, all of which militate against a diagnosis of epidermolysis bullosa hereditaria.

DR. HOWARD FOX: I would like to know whether Dr. Traub has examined the patient for stigmas of hysteria, such as corneal anesthesia or absence of pharyngeal reflex.

DR. TRAUB: Such examination has not yet been made.

SARCOID OF CIRCINATE TYPE. Presented by DR. HOWARD FOX.

Mrs. C. H., aged 62, born in the United States of American parents, had first noticed an eruption on her forehead four and a half years previously; other regions of the face were involved later. There were half a dozen lesions, varying in size from that of a pea to that of a dime, on the forehead, one on each temple and on the upper lip, and several smaller ones on the chin. All of the lesions were dry, superficial, flat plaques or rings, the latter consisting of dull reddish borders with moderate fine whitish scales and apparently atrophic centers. No nodules of lupus vulgaris could be detected by diascopic pressure. There was no evidence of itching. The patient said that she had been treated by the roentgen rays, ultraviolet rays, electrolysis, ointments and arsenic without any benefit. She had recently been given twelve injections of a gold compound and sodium thiosulphate without result. Histologic examination of one of the lesions showed "sarcoid of mixed Boeck and Darier-Roussy type." The patient was a small, slender woman apparently in good health.

MELANOMA. Presented by DR. HOWARD FOX.

T. de R., a woman, aged 22, had suffered from a lesion on the tip of the nose for the past two years. It was said to be slowly increasing in size. It was the size of a pinhead, slightly elevated, bluish, firm, smooth and free from hairs. There had been no treatment.

DISCUSSION

DR. WISE: Is this considered a potentially dangerous lesion?

DR. BURNETT: It is not increasing in size, and I should leave it alone.

DR. HOWARD FOX: Dr. Pusey considers this to be the dangerous type of pigmented mole.

DR. MACKEE: I agree that it is the so-called black mole and is potentially very dangerous. It can be lighted up by the application of caustics or by any treatment that does not completely destroy the lesion. In this location, it will not be subjected to irritation, and I think that it would be safe to leave it alone, assuming that it will be left absolutely alone, provided the patient remains under observation. However, because of the danger of bad advice and improper treatment, I prefer total destruction. It can be excised by a good surgeon, leaving a scar that would not be disfiguring. It could be removed by diathermy but that would leave a bad scar. Radium is not very efficacious in quiescent cases, but if they show activity a small proportion of them will yield excellent results. I prefer radical excision.

DR. LANE: The lesion on the nose is not active. I believe that it is unwise to leave a black pigmented mole of that sort alone until it shows signs of activity. I have never seen any ill results follow the destruction of a quiescent mole of that sort, neither have I seen any good results from removal of such a lesion after it had started to grow. After that, metastasis and death always occur. The lesion is so potentially dangerous that it ought to be destroyed, and no treatment that does not completely destroy it at once should be used.

DR. FRASER: I agree with Dr. Lane in what he said about leaving such lesions until there are manifestations of activity; as a rule, if one waits that long, no treatment is of any avail. This lesion should be removed at once with the endotherm knife.

DR. HOWARD FOX: If the patient consents, I shall have this lesion removed by the knife.

MORPHEA OF PREPUCE. Presented by DR. HOWARD FOX.

E. H. D., a business man, aged 38, had suffered from the eruption for thirteen months. It had gradually increased in size since then and formed a band ¼ inch in width, confined to the prepuce for half of its circumference. It was situated mostly on the mucous surface, extending slightly on the cutaneous portion of the prepuce, was smooth, pearly white and firm to the touch and was surrounded by a faint pinkish border. In the center of the lesion there was a dark brown freckle, the size of a pinehead. The lesion caused some discomfort during intercourse. There had been no treatment. The basal metabolic rate was minus 6.

DISCUSSION

DR. WHITEHOUSE: The lesion is on an unusual location. I do not see why circumcision would not remove it entirely.

DR. TRAUB: If removed by circumcision, is there an increased likelihood that the resultant scar would develop the same condition and cause a worse contraction?

DR. HOWARD FOX: Circumcision is the treatment that I recommended, but the patient seemed rather loath to have it done. Examination of the prepuce shows that it would be possible to remove the lesion completely by this means.

MORPHEA. Presented by DR. HOWARD FOX.

R. K., a schoolgirl, aged 12, presented an eruption of thirteen months' duration. It consisted of a bandlike lesion 1¾ inches long by ¾ inch at the widest part. The lesion extended from a point immediately below the lobule of the left ear, downward and forward in a narrow tail-like prolongation. It was yellowish white, smooth and deeply infiltrated, and had a well marked lilac border. There had been no treatment. The patient was well nourished and of a healthy vigorous appearance. Her basal metabolism was normal.

LUPUS ERYTHEMATOSUS DISSEMINATUS. Presented by DR. HOWARD FOX.

J. A. S., a contractor, aged 41, had suffered from a generalized eruption for nine years. In 1926, it disappeared temporarily for one year, while he was living in Florida. The eruption began on the heel, and soon after this he was operated on for appendicitis which was followed by ether pneumonia. Before leaving the hospital, the generalized eruption appeared. It affected the face, neck, forearms, back of the hands and to a slight extent the abdomen and back. The eruption, in general, was superficial with a tendency to the formation of diffuse areas. Some of the patches were fairly well defined, while others faded gradually into the normal skin. Various shades of red predominated. There was a moderate fine scaling of the adherent type. There were peculiar zigzag areas on the forearms of a type seen in lichen planus. The lips were dry and showed whitish scaling. None of the lesions showed evidence of scratching. The patient had had an operation for hemorrhoids seven years before presentation and his tonsils had been removed in childhood, though he suffered occasionally from sore throat. He had one abscessed tooth. He was well nourished and in good general health. He smoked cigarets moderately and drank no alcohol. Examination of urine and stools and general physical examination showed nothing abnormal other than the eruption. The patient was firmly impressed with the idea that a year's rest in Florida with

"freedom from worry" was responsible for the remission in his disease. He also thought that arsenic had had a favorable effect. He had recently been treated by a gold compound and sodium thiosulphate with marked benefit.

A histologic examination was made by Dr. Highman, who reported that the sections "suggested lupus erythematosus disseminatus or erythema perstans."

DISCUSSION

DR. COMBES: I agree with the diagnosis. I think that the lesions on the outer borders of the feet are suggestive of lupus erythematosus. I have had a patient with a similar case with lesions in the same location, which were extremely tender, such as these lesions are.

DR. WHITEHOUSE: I agree with the diagnosis as made, but I cannot reconcile the accompanying bullae or blisters on the feet. It may be simply from pressure or traumatism; I do not know of any other origin.

DR. MACKEE: I think that the entire eruption is lupus erythematosus.

LICHEN PILARIS SEU SPINULOSUS. Presented by DR. HOWARD FOX.

G. F. N., a business man, aged 40, born in the United States, was seen for the first time three weeks prior to presentation. He then stated that the eruption had appeared six months previously, one month after he had been in Florida and had acquired a deep tan on the greater part of his body. The eruption had attained its maximum development within about three months. It was symmetrically developed on the lower part of the back, buttocks, arms, forearms and thighs. The lesions were somewhat more prominent on the extensor than on the flexor surface of the upper extremities, although the entire circumference was affected. The eruption consisted of discrete, noninflammatory, flesh colored, follicular plugs, which felt like a nutmeg grater on palpation. Some of them showed slight filiform prolongations. There were no subjective symptoms. No other members of the family had been similarly affected. The urine was normal, and the Wassermann reaction was negative. The patient was a well built, athletic appearing man of neurasthenic type. He had recently used green soap and salicylic acid ointment, with marked improvement.

LUPUS ERYTHEMATOSUS OF THE LIPS. Presented by DR. MALONEY.

A. E., a man, aged 35, born in Mexico, presented a scaly eruption on both lips with some atrophy. This began six years previously as a red spot on the lower lip which gradually spread, causing redness, edema and scaling of both lips. He had been treated with the roentgen ray for several months three years before presentation. He had had seventy injections of a gold compound and sodium thiosulphate in doses of from 50 to 100 mg. (six doses of 100 mg.), with considerable improvement.

Suggestions as to treatment were requested.

DISCUSSION

DR. WHITEHOUSE: I agree with the diagnosis.

DR. TRAUB: It is difficult to offer any suggestions for treatment in this case because the lesions are on the mucous membrane. I only wish to warn against any irritating local applications because of the great danger of producing a malignant disease. Considering the large number of injections of a gold compound that have been given, it might be well to give a series of injections of sodium thiosulphate and at the same time have the patient take gold chloride in tablet form.

DR. HOWARD FOX: I should like to ask whether any one has treated a patient with lupus erythematosus of the lips with a gold compound and sodium thiosulphate.

DR. LANE: In reply to the request for information as to results of treatment of lupus erythematosus of the lips with a gold compound and sodium thiosulphate, I can report one case in which the whole lower lip was affected, which promptly recovered with about twenty injections of this drug.

DR. MACKEE: I used the treatment with a gold compound in the case of a woman with lupus erythematosus of the lip extending a little on the skin, but there were no patches on other parts of the body. The eruption disappeared after twenty injections and has not recurred during a period of two years.

DR. HOWARD FOX: I would like to make a therapeutic suggestion. In some of our cases, in which the involution of the lesions under therapy with a gold compound was somewhat slow, we have found that better results were obtained when in addition to the treatment with a gold compound very mild freezing with solid carbon dioxide was used.

DR. WISE: Both Dr. Jadassohn and Dr. Bloch recommended the use of silver arsphenamine as an aid to injections of a gold solution in cases of lupus erythematosus which proved to be recalcitrant to the treatment with a gold compound.

DR. COMBES: I wish to substantiate what Dr. Fox has said regarding the quicker response of lesions to local treatment when gold sodium thiosulphate is used. In one case which I recall, with lesions of the oral mucous membrane and skin of the cheeks, the latter cleared up on treatment with the gold compound but the former did not. However, with weekly applications of 15 per cent chromic acid in conjunction with the gold compound, the lesions responded promptly.

DR. MALONEY: The patient lives in Mexico City and his treatment would have to be carried out there. He is not under my observation all the time. I imagine that he has had eight small doses of the roentgen ray and has had no injury from them.

MYCOSIS FUNGOIDES. Presented by DR. TRAUB.

E. S., aged 44, was born in the United States. His first skin trouble dated back ten years, at which time he consulted and was treated by several physicians for a condtiion diagnosed as psoriasis or parapsoriasis. The condition had been more or less progressive, irrespective of treatment, and within the last year or two the patient's general health had been markedly affected; he had lost weight and was very nervous and generally run down. He had been sent to Dr. Williams because of a large tumor which had developed on the lower part of the abdomen and which was presumed to be malignant.

The patient had received roentgen treatments over the so-called psoriatic areas but had not received such treatment on the lower part of the abdomen.

In addition to the mass on the lower part of the abdomen, several small early tumors could be noted in the stage of development, particularly on the extremities. Itching had not been a marked feature in the case. As the patient had been seen only once, no laboratory work was yet available.

DISCUSSION

DR. HOWARD FOX: The case was especially interesting to me as I had reported a case of mycosis fungoides in the infiltrative stage in a man who has suffered from psoriasis for twenty-eight years. He had been seen for many years at the Vanderbilt Clinic by Dr. Jackson and others, who considered it an ordinary cases of psoriasis. Finally, the character of the lesions changed and it became evident that it was not an ordinary psoriasis. Histologic examination showed multiplicity of cells in the cutis which would not be consonant with psoriasis, and the diagnosis of mycosis was made. In the case presented, there was a tendency to circination, which is also common in psoriasis, but there was too much infiltration for an ordinary case of psoriasis. The presence of the larger tumor on the abdomen

and its rather short duration strongly favor the diagnosis of mycosis fungoides. I think that a histologic examination would settle the question without a doubt.

DR. WISE: I presented a patient before this Society several years ago, who had had typical psoriasis for twenty years and who subsequently developed mycosis fungoides at the site of the psoriatic lesions. The diagnosis of mycosis fungoides was confirmed by microscopic examination.

DR. COMBES: I do not see how you can suppose a pre-existent, psoriasis without a biopsy. Mycosis might follow on psoriasis, although I have never seen a proved case. However, there is no reason why a premycotic eruption cannot take on the clinical appearance of psoriasis, analogous to the psoriasiform variety of other dermatoses, and still be mycosis fungoides rather than true psoriasis.

DR. WHITEHOUSE: I agree with Dr. Fox and Dr. Wise. We do not see these cases now as we did, but there is a type of mycosis fungoides that gives the appearance of psoriasis for many years. I think that it is mycosis fungoides; in cases of eczema, patients have had what seemed to be eczema for many years, subsequently infiltration takes place, and finally the fungoid tumors form and break down. I do not think that the condition is psoriasis. I think that it is the type Dr. Wise spoke of, and that these lesions are mycosis from the beginning.

DR. MACKEE: I think that it is a case of mycosis fungoides preceded by a long period of psoriasiform type of prefungoid lesions. The case and the discussion bring up the question of the identity of disease. We see cases of psoriasis — clinically and histologically psoriasis — and later they turn out to be mycosis fungoides. I agree with Dr. Wise that cases like that are mycosis from the beginning; but, nevertheless, in the early stage they are psoriasis as far as can be ascertained. Therefore, does psoriasis change to mycosis fungoides, does the patient have both diseases or is the supposed psoriasis mycosis fungoides from the beginning? It is, of course, possible for a patient to have both diseases, but in all recorded cases the patient has ceased to have psoriasis after a diagnosis of mycosis fungoides has been established — and psoriasis is a disease that seldom disappears completely for a period of many years. It is my opinion that these cases are mycosis fungoides from the beginning, in spite of clinical and pathologic diagnosis of psoriasis, and that at times it is impossible to identify beyond any possibility of error even a well established dermatologic entity with any means at our disposal at present.

DR. LANE: I have no doubt that this is a case of mycosis fungoides and has always been such. There seems to be no reason why psoriasis and mycosis fungoides might not exist together in the same patient, but as far as I have been able to learn no one has seen this occur when there was not some doubt about the diagnosis of two diseases.

DR. MACKEE: Of course we may have a coincidence of psoriasis and mycosis in the same patient; that has not been observed, but it is conceivable; but, assuming that Dr. Lane is correct, that you can have psoriasis and change to mycosis, what becomes of the psoriasis? We do not see any cases of mycosis fungoides in which the psoriasis continues. Does mycosis fungoides cure psoriasis? I venture to say that in this case the psoriasiform lesions will disappear and all the lesions will assume the characteristics of mycosis fungoides.

DR. FRASER: I distinctly recall having seen early lesions of mycosis fungoides which looked like psoriasis and which could not be distinguished histologically from psoriasis. In the case under discussion the lesions bear a superficial clinical resemblance to psoriasis, but on close inspection it is not difficult to see that the whole picture is that of mycosis fungoides. I believe with Dr. Whitehouse and Dr. MacKee that the cases of mycosis fungoides reported in the literature as mycosis fungoides developing on psoriasis were probably mycosis from the beginning.

DR. HOWARD FOX: I do not think that the question argued by Dr. Lane and Dr. MacKee can be settled. In the case of my own which I quoted, I do not

know whether the original eruption was psoriasis which had changed to mycosis or whether the eruption that had existed for so many years was actually mycosis of the psoriatic type. I merely meant to say that the case had been considered an ordinary one of psoriasis in which no one had dreamed of performing a biopsy to confirm the diagnosis.

BASAL CELL EPITHELIOMA. Presented by DR. RULISON.

W. P., a stonecutter, married, born in this country of Bohemian parents, from the Cornell Clinic, did work that exposed him to marble dust and chips. He first visited the clinic on March 25, 1929. The duration of the trouble was six years. The lesion was located in the skin around and above the left nipple, forming a round, red, scaly and crusted area approximately 3 inches in diameter, with a slightly raised and pearly, indurated border along parts of the edge. There was a raised, hard growth, the size of a dime, with a pearly border at the lower central edge of the large area.

A small part of the growth was removed for microscopic examination. The pathologic diagnosis (Dr. Fraser) was basal cell epithelioma. The lesion had failed to respond favorably to intensive treatment with the roentgen ray.

DISCUSSION

DR. MACKEE: Ordinarily, a lesion of this sort would have disappeared under the influence of the treatment it has received. Because intensive roentgen treatment was unsuccessful, I wonder if this is a true basal cell epithelioma. I understand that about 12 or 15 per cent are not true basal cell epitheliomas, and it is approximately that percentage that responds less well to the roentgen ray and to radium. Cases in this group may contain some prickle cells, or may be derived from a layer above the basal cell layer, the so-called cubocellular epithelium, or the cells may be of the undifferentiated type.

DR. FRASER: The case was reported as being basal cell epithelioma. There are different types of basal cell epithelioma. The great majority have their origin from a hair matrix; another type comes from the sweat duct epithelium; this type is more resistant to treatment, and is more likely to return after removal than the tumor of the hair matrix. Metastases have been known to occur in the sweat duct type. All epitheliomas arise from the growing cells, and the difference between a true prickle cell and a basal cell epithelioma is that the prickle cell epithelioma arises from cells which tend to differentiate into corneus epithelium, whereas the so-called basal cell tumors arise from cells which differentiate to form the appendages, such as hair follicles and sweat ducts.

DR. MACKEE: I should like to ask Dr. Fraser whether this case would fall in the clinical category of superficial epitheliomatosus cutis, in which the lesion starts as a scaly macule and spreads peripherally with a pearly, rolled border. These eruptions have often been confused with Paget's disease or Bowen's cancer. In many of these very early cases of superficial basal cell epithelioma, if the tissue is removed from the advancing margin, one sees a budding of the basal cell layer of the epidermis but not of the appendages, and the proliferation forms a basal cell epithelioma with no suggestion of newly formed or partially formed appendages, such as one sees, for instance, in tricho-epithelioma.

DR. FRASER: Under normal conditions of development these cells are destined to form hair follicles.

DR. MACKEE: I would suggest that no more roentgen or radium treatment be given. The lesion should be thoroughly cureted and then treated with electrocoagulation and electrodesiccation, or it may be excised.

DR. LANE: I favor excision.

ATLANTIC DERMATOLOGICAL CONFERENCE: NEW YORK, NEW ENGLAND, PHILADELPHIA AND BALTIMORE-WASHINGTON DERMATOLOGICAL SOCIETIES

J. FRANK FRASER, M.D., *Secretary*

New York, Dec. 6, 1929

PAUL E. BECHET, M.D., *President*

DERMATITIS VENENATA. Presented by DR. WISE.

J. F., a photographer, aged 27, from the Post-Graduate Skin Clinic, with no allergic history, began working with chemicals ten years before presentation. Two years before presentation an eruption started on the forehead and later spread to all parts of the body. In 1928, when the patient went to the mountains the eruption disappeared, but reappeared when he returned to work. In April, 1929, he went to Florida and the eruption cleared up in a few days; it reappeared two weeks after he returned to work. In July, 1929, he went away again and the eruptions on his face cleared up, but this time there was no improvement on the body.

The patient presented a generalized eruption, the appearance resembling mycosis fungoides; his chief complaints were extremely severe itching and insomnia. Biopsy and tests at the Vanderbilt Clinic were not decisive according to the statement of the patient. Later contact tests with photographic developers (Metol, etc.) were alternately negative and positive.

The patient had had roentgen treatments and ultraviolet exposures; also injections of sodium thiosulphate and calcium without improvement, but he had improved greatly since hospitalization, which had been for one week, and proper local applications.

DISCUSSION

DR. BLOSSER: I was interested in the case and asked the patient what chemicals he worked with. The list is as follows: sodium thiosulphate for fixing; a developer containing metol hydroquinon, sodium carbonate, sodium sulphite, potassium bromide, oxalic acid and pyrogallol; also ammonium bichromate and ferrous cyanide for bleaching. How is one to decide which of these chemicals the patient is sensitized to? He told me that on the first examination he had had positive reactions to tests of two or three of the chemicals; on the second test, the reactions were all negative. He brought in all the chemicals which he had been using and had tests made with them. I think we may have to adopt a different idea about certain chemical dermatoses. They may not be specific reactions to one or more chemicals, but may be produced by long continued contact between a number of these irritants and the skin.

DR. WEIDMAN: I do not think this in an exogenous dermititis. The distribution, the intense generalized itching, together with certain other characteristics in the lesions themselves make it seem rather endogenous and coming within the group of erythema perstans. Some of the lesions are oozing around the edges; it may be in line with what has been called Wende's disease, which progresses into something like dermatitis herpetiformis.

DR. STOKES: I would support Dr. Weidman's suggestion in favor of a diagnosis of dermatitis herpetiformis. There are groups of lesions on the abdomen distinctly suggestive of dermatitis herpetiformis. I believe that there is some possibility of a limited relief for the patient in that direction.

MELANOMA. Presented by DR. MACKEE.

C. M., a chauffeur, aged 28, presented lesions on the upper left portion of the forehead, trunk and thighs, which had been present since birth. He was first seen at the Post-Graduate Skin Clinic on Aug. 28, 1929, presenting in the upper left

corner of the forehead, a mass about the size of a bean, verrucous in character, excepting the upper part, which was somewhat smooth and slate-colored. This was removed by bipolar diathermy, and under microscopic examination showed epidermic nevus with pigment. Subsequent to this, numerous subcutaneous lesions developed, varying in size from that of a pea to that of a bean, the larger ones being attached to the overlying skin.

MYCOSIS FUNGOIDES. Presented by DR. WISE.

G. B., aged 45, when seen on October 4 at the Post-Graduate Skin Clinic, presented infiltrated bluish-red plaques on his face, neck and scalp. The patches varied from the size of a nickel to that of a silver dollar. There were large, confluent, bluish-red and scaly areas on other parts of the body, especially the arms. The clinical diagnosis of mycosis fungoides was confirmed by the histologic picture. The eruption had started approximately a year previous to presentation.

The case was presented to show the marked improvement in the condition of the skin after roentgen treatment. Most of the elevated lesions had entirely disappeared.

On presentation, the skin exhibited a diffuse red, infiltrated condition, most pronounced on the extremities, resembling the "homme rouge" of the French writers. Itching had stopped after the course of roentgen treatment, and the patient had gained in weight and strength.

A CASE FOR DIAGNOSIS (MACULAR ATROPHY). Presented by DR. MACKEE.

C. P., a silk-worker, born in the United States, from the Post-Graduate Skin Clinic, presented lesions of three and a half years' duration. He was first seen on March 2, 1929, when he exhibited lesions on the back of the neck, trunk and on the arms, and one lesion just in front of the left ear. These lesions were round and varied in sizes from about ½ to 2 inches in diameter. They were sharply defined; some were slightly elevated, and some were flat; their color varied from that of normal skin to a violaceous hue. The larger lesions presented a marked violaceous border; some of the lesions showed well marked clinical atrophy, and the elevations could be easily depressed. There was no history of the ingestion of drugs or local applications. Examination of the tissue for phenolphthalein gave negative results. The Wassermann reaction was negative.

Microscopic examination by Dr. Satenstein showed an edematous cutis and a perivascular lymphocytic infiltration fairly well limited. There was a disappearance of the elastic tissue in the subepidermic zone and a splitting up of the elastic tissue elsewhere. The diagnosis made was that of an edematous stage of an atrophic process.

DISCUSSION

DR. STOKES: To me, this is one of the most interesting cases shown. I am in favor of a diagnosis of the so-called multiple, benign, tumor-like new growth of Schweninger and Buzzi. I have not reviewed the literature, but Schweitzer's report in 1922 is the latest that I recall. At least there are some lesions in this case which conform to the example of the process which I saw during my association with Dr. Pusey.

DR. WEIDMAN: Whatever the name may be that is applied, clinically and pathologically, the process is primarily a degeneration of the skin. A feature which has not been investigated and is simple to approach is the nature of the fluid substance in the lesion—whether or not it will give a reaction toward mucin. The process appeals to me as mucoid degeneration; if that is the correct diagnosis, one should give attention to the thyroid. The lesion on the cheek was different from that on the scalp; and all that trythema means more than a simple degenerative process present. Whether that is due to more intensely acting products, or a stimulation by the by-products of degeneration, we do not know.

LEPROSY. Presented by DR. MACKEE.

T. H., aged 23, a student from the Philippine Islands, presented lesions of three months' duration on the face and arms. He was first seen at the Post-Graduate Skin Clinic, on Oct. 5, 1929, when he presented discrete, macular, discoid lesions about the size of a fifty cent piece and smaller, with hyperpigmented borders and slight infiltration; also a long painful swelling on the left side of the neck beneath the skin. Both ulnar nerves were enlarged, being easily palpable. A smear from the mucous membranes showed organisms resembling Hansen's bacilli. Microscopic examination of one of the lesions showed leprosy, with a nodular arrangement suggesting sarcoid. Smears from the tissue were positive for the leprosy bacillus. The Wassermann tests were negative. Treatment with chaulmoogra oil products resulted in improvement of the lesions.

LEPROSY IN HUSBAND AND WIFE. Presented by DR. HOWARD FOX.

I. K., a man aged 56, and G. K., his wife, aged 52, came to the United States from Russia in 1904. Mrs. K. first noticed anesthesia of the hands in 1918, following a burn. In 1927, the nodular lesions appeared. At presentation she was suffering from a moderately advanced nodular leprosy affecting chiefly the extensor surface of the upper extremities. There were also a few lesions, both macules and papules, on the trunk and lower extremities. The face, however, was free excepting for slight infiltration about the eyebrows and of the ear lobules. The ulnar nerves were enlarged, and there was partial anesthesia of the upper extremities.

Mr. K., a carpenter, first noticed an eruption in 1927. When first seen, six months before presentation, he presented several patches of typical maculoanesthetic leprosy confined to the left forearm. The lesions were distinctly anesthetic, dull reddish-brown, smooth, and without appreciable infiltration. The ulnar nerve of the same side was greatly thickened and less sensitive than normal. There was wrinkling of the skin on the backs of the hands, and atrophy of the interosseous muscles. There was slight contracture of the fourth and fifth fingers. Nasal smear was negative for bacilli. The patient had improved greatly under treatment with chaulmoogra oil, and when presented the eruption was barely visible. There was some ankylosis of the left elbow, due to a fracture when he was 3 or 4 years of age.

Since the patients' arrival in the United States in 1904 they had lived constantly in New York or that vicinity. The question arose as to whether or not the husband contracted the disease from his wife while living in or near New York City, or whether he had become infected while in Russia. The apparent incubation period in the wife was about fourteen years.

VON RECKLINGHAUSEN'S DISEASE (TWO CASES). Presented by DR. MALONEY.

CASE 1.—A. B., aged 43, was born in the United States of German and Irish parents. She first noticed the eruption about twenty-three years previous to presentation, after the birth of her first child. She was the mother of twelve children, eight of whom were living and well. Her parents had died at an advanced age. No relative had ever suffered from a similar disease. The development of the eruption had been gradual until, as presented, there was an extremely profuse eruption of tumors scattered over almost the entire cutaneous surface, including the scalp, face, neck, trunk and extremities. There were also a few lesions on the palms and the soles. The eruption consisted mostly of tumors, and to a slight extent, of freckle-like pigmentation. The tumors were discrete, though closely aggregated in many regions, and varied in size from that of a pinhead to that of a large English walnut. The majority were of flesh color; some were of a yellowish or bluish tint, some were sessile, others pedunculated. The consistency was, as a rule, semisolid or soft. A few of the tumors had

comedo-like openings from which cheesy material could be expressed. There was some tenderness on manipulation.

The patient was a small woman, weighing about 100 pounds (45.4 Kg.), and was of a dark complexion. She looked pale and delicate, and her mentality seemed somewhat below the average. It was estimated that there were more than 2,000 tumors on the back.

CASE 2.—R. N., a widow, aged 55, was born in Austria and had suffered from the eruption for twenty years. The eruption was confined to the back and extremities, and consisted of freckle-like and larger pigmented macules and tumors varying in size from that of a pinhead to that of a pigeon's egg. The majority were sessile; some were pedunculated, and all were painless. The patient appeared to be in fair general health, and her mentality seemed normal.

LUPUS VULGARIS (EXTENSIVE). Presented by DR. HOWARD FOX.

J. P., aged 46, a dress finisher, had suffered from an eruption for twenty years. She had had measles and scarlet fever as a young child. There was no family or personal history of tuberculosis other than the eruption of the patient. The disease involved almost the entire left leg from the knee to the toes. There was considerable scaling, crusting and infiltration, though individual apple-jelly nodules were apparent. Only a few areas of normal skin were to be seen. A palm-sized ulceration had appeared on the outer aspect of the central part of the leg about eighteen months previously and radium therapy had been given with marked benefit. There was a small patch showing apple-jelly nodules on the right cheek, which had been present for three months. There was no involvement of the nose or mouth.

Histologic examination showed a typical structure of lupus vulgaris. The Wassermann test was negative, and the tuberculin test positive. A roentgenogram of the chest showed nothing abnormal. A roentgenogram of the legs showed some absorption of lime salts in the bones of the feet, more evident on the left side. The knee joints, the tibiae and fibulae were normal. The patient appeared to be in good health.

DERMATITIS VENENATA (SOUR DOUGH). Presented by DR. WISE.

A man, aged 21, had been a baker for four years, working with sour dough. He presented an itching, scaly, eczematous dermatitis which had started on the right hand five weeks previously. There had been no eruption prior to that. The skin contact test with sour dough was positive. All other tests with various flours, oils, malt, etc., were negative. The flour did not seem to irritate the skin when dry, but only when mixed in dough form.

DISCUSSION

DR. WEIDMAN: This patient has come from Germany very recently, and from there has also come a very large literature by Benedek on *Schizosacchromyces hominis*. This author has found this fungus in a tremendous number of cases of what appear to be ordinary eczema. Some doubt has been cast on his cases as to whether it is a "laboratory infection" or not, but the fact that the sour dough contact test appeared in a patient working in a class of material which supports yeastlike fungi perhaps strengthens the idea that there may be at least some other yeast species in this dermatitis.

URTICARIA PIGMENTOSA. Presented by DR. WISE.

B. M., a girl, aged 6 years, presented an almost universal, typical urticaria pigmentosa which had appeared at the age of 6 weeks. The interesting feature of the eruption was the presence of striped pigmented lesions running longitudinally around the neck, in the form of narrow bands.

XANTHOMA TUBEROSUM MULTIPLEX. Presented by DR. TRAUB.

L. C., aged 34, a housewife, born in the United States, presented an unusually widespread eruption of typical xanthoma tuberosum of three years' duration. A diagnosis of hypoglandular disturbance was made, of the hypothyroid type, and the patient was put on a low fat and carbohydrate diet. She lost 12 pounds (5.4 Kg.) on the first six weeks of the diet, but none following that time. On Sept. 16, 1929, she was given 2 units of insulin subcutaneously, and to the date of presentation had been taking 6 units. Her blood pressure was 108 systolic and 78 diastolic. Chemical examination revealed:

	NACL	Sugar	Urea Nitrogen	Uric Acid
Aug. 29, 1929.....	487.6	93.4	14.1	4.15
Sept. 9, 1929.....	528.3	100.4	19.3	4.1
Oct. 25, 1929.....	487.6	113.8	14.8	8.55

	Whole Blood	Serum	Plasma
Sept. 9, 1929.....	...	554	...
Oct. 25, 1929.....	303	468	431

DIFFUSE IDIOPATHIC ATROPHY. Presented by DR. BECHET.

J. T., aged 43, stated that she had first noticed her dermatosis ten years previous to presentation. Up to the time that she had applied to the clinic she had never been free from the lesions, new patches constantly appearing as the older ones faded out. These patches appeared anywhere on the body; there seemed to be no site of predilection. Frequent observation over the space of a year demonstrated an eruption with many peculiar characteristics. Patches at the height of evolution were sharply outlined, flat, and bright red. Later on, the bright red changed to duller red, with evidences of capillary dilatation; still later, involution showed slightly brownish patches with very superficial atrophy and dilated capillaries. The oldest lesions showed only a simple, very superficial atrophy. A few patches on the leg consisted of hemorrhagic puncta, slightly suggestive of Majocchi's disease. The skin on the thighs was translucent, and superficial veins and arterioles were plainly visible. Section showed a very thick epidermis with marked acanthosis. The connective tissue was edematous, and there appeared to be an increased number of blood vessels with hyperplastic walls, about many of which there was a slight cellular infiltration which was lymphocytic.

A CASE FOR DIAGNOSIS (DERMATITIS FACTITIA). Presented by DR. SCHWARTZ.

Mrs. L., aged 27, was first presented at the New York Dermatologic Society on Nov. 28, 1929. The Wassermann reaction was negative. Four intravenous injections of neoarsphenamine and four intramuscular injections of bismuth were given without apparent effect on the appearance of the lesions. Sections were removed from two lesions for study. Bacteriologic and histologic examinations were negative; the results of the chemical examination of the blood, including the blood count, were normal; the urinalysis was negative. A psychiatric examination failed to find a definite lead which would substantiate the assumption that the skin lesions were artificially produced.

DISCUSSION

DR. TOWLE: In 1907, I published the reports of four cases under the title of "Gangrena Cutis Hysterica." This case reminds me very strongly of those. Such cases occur mostly in girls who are hysterical. Therefore, it might be well to send the patient to a neurologic clinc for investigation from that point of view. She was quite talkative, and that, too, is characteristic. She said she had had pneumonia for two years, which is also interesting. All of these facts lead to the conclusion that she is below par physically and also that she has hysteria.

These hysterical patients are honest when they say they did not cause the lesion. Janet has written a wonderful description of hysteria, and explains it on the basis that hysterical people are peculiarly apt subjects for hypnosis, which is essentially a matter of suggestion. Suggestions act very easily on this type of patient. In hysteria there is a state or condition known as somnambulism. This state may be defined as that hysterical state in which an idea or a feeling takes on an exaggerated growth which the patient is powerless to check. Because of this unchecked growth outside of the control of the will, that one idea acquires such importance that it finally dominates the patient's complexity. The dominant idea becomes disassociated from all other functions and controls. Now, the suggestion which finally becomes the one dominating idea may come from within or without. The sight of an injury or wound or the hearing of a story may be enough to supply the suggestion. Once received, it will grow and grow until it rules. Then in the somnambulistic state the patient tries to reproduce the wound. Emerging, she has no memory of how it came and therefore can honestly deny all knowledge. I would therefore recommend that this girl be studied further in the psychiatric clinic.

DR. SMITH: I agree with Dr. Towle in believing the lesions to be probably factitious.

DR. BLAISDELL: This case appeals to me as being probably factitious. The fact that keloids resulted on some of the lesions verifies this theory, and suggests that either an acid or an alkali is being used. Of course, the usual method of detecting such self-inflicted injuries is by means of the sealed dressing. I have found in several cases of this sort that an analysis of the used dressing, whether sealed or not, will reveal the nature of the material which the patient is applying.

DR. STOKES: I concede the importance of Dr. Towle's observation that she is garrulous and inclined to assume the center of the stage. She is, however, subject to frequent colds, gained weight rapidly following an attack of pleurisy, and then the lesions began to appear. She therefore conforms to some extent to the fat type of tuberculous person, usually a woman, who has a high resistance to the disease. She is, perhaps, in an allergic state and reacts with violence to the deposition of a few organisms in her skin from some glandular focus, producing the extremely destructive lesions here observed. One of the lesions is strongly suggestive of tuberculous condyloma which one sees in countries where the disease is more common than in the United States, and the localization is certainly satisfactory for Bazin's disease. On the other hand, as has been pointed out, the occurrence of keloids, particularly on the right elbow, is strongly suggestive of a burn element in the etiology, and thus of self-infliction.

DR. SCHWARTZ: We considered seriously the question of the condition being an artefact, but could get no support for that from the neurologic or psychiatric examination.

DERMATITIS MEDICAMENTOSA (PHENOLPHTHALEIN). Presented by DR. ELLER.

G. B., a shipping clerk, aged 17, from the Post-Graduate Skin Clinic, developed the eruption over the trunk six months previously. The eruption had persisted, the lesions gradually increasing in size. There were numerous, rounded, brownish-violaceous, pigmented lesions in various sizes from that of a pea to that of a dollar, over the chest, abdomen, back, shoulders, thighs and the lower lip. At irregular intervals during the six months, a redness developed about the pigmented lesions. Later, each lesion appeared to be larger. This occurred as often as once a week. The longest period without erythema was one month. The patient had been taking various laxatives containing phenolphthalein at irregular intervals. When first seen there was a distinct erythematous halo about each pigmented lesion. The patient's mother had given him one "feenamint" tablet at bedtime the night previously. The erythema had disappeared in two days.

XANTHOMA MULTIPLEX RESEMBLING URTICARIA PIGMENTOSA. Presented by DR. HOWARD FOX.

H. P., a girl, aged 3, presented numerous patches from the size of a pea to that of a dime, over the face, neck, trunk and extremities. These lesions were irregular, slightly elevated, and of soft consistency. Some showed a tendency toward fusion. They were yellowish brown. Friction applied to these lesions produced no edematous or trythematous reactions. The histology was that of xanthoma.

PITYRIASIS ROSEA OR SYPHILIS. Presented by DR. HOWARD FOX.

P. E., a white chauffeur, aged 22, born in the United States, presented an ulceration of the distal phalanx of the left thumb, and a generalized macular eruption covering the neck, the trunk, the upper extremities and the thighs. The eruption, though generally macular, showed in areas oval patterns and fine scaling. Generalized adenopathy was present with glandular enlargement, most conspicuous in the left axilla. The ulceration of the finger was of seven weeks' duration, resulting from an injury received in a brawl. The eruption on the body had been present three weeks. The Wassermann test was negative, as was also the Kahn precipitation test.

NOTE.—The patient has received no antisyphilitic treatment. A month after presentation, the eruption had entirely disappeared, most of the lesions having become scaly and distinctly oval in outline before disappearing. A roentgenogram of the left thumb disclosed an osteomyelitis of the distal phalanx.

DISCUSSION

DR. SCHAMBERG: The case is a very interesting one because of the negative Wassermann reaction. The patient has a generalized macular eruption over the body and extremities, and an indolent ulcerated sore on the thumb. There is a scaly discoid patch on the arm. I believe that the case is one of syphilis, despite the negative Wassermann test. The eruption is quite uniform in its elements and it does not tally at all with the eruption in pityriasis rosea. Then, too, the development of the lesion on the finger is extremely suggestive. The man had a fight and struck a pin; a sore developed which in a few days became progressively worse for several weeks, and then this eruption developed, which is in harmony with the picture of syphilitic infection. If it is syphilis, why should he have a negative Wassermann reaction? First, we cannot exclude the possibility of laboratory error. Secondly, in a small percentage of cases of syphilis there is no reagin in the blood in early syphilis, and the Wassermann test may be negative. The case should be studied further with complement-fixation tests to determine whether the Wassermann reaction does not become positive.

DR. SMITH: I should like to endorse what Dr. Schamberg has said. I think that this case will prove to be syphilis. It is an unusual eruption for pityriasis rosea, as there are no typical lesions such as one would expect in pityriasis rosea which has lasted for three weeks. As far as the negative Wassermann reaction is concerned, there is nothing to add to what Dr. Schamberg has said. The case needs further study, and I believe that it will prove to be a case of syphilis, the sore on the thumb being the primary lesion.

DR. STOKES: Of course, the eruption is not necessarily that of secondary syphilis. Morphologically, it is suggestive. I failed, however, to find any distinctive satellite bubo from the lesion on the thumb, either at the epitrochlea or in the axilla. I should like to know if any dark-field examination has been made. If only one Wassermann test of the blood has been taken it should be repeated, and treatment should not be begun before the condition has been definitely diagnosed, unless one is prepared to commit himself to the diagnosis by the act of treating the patient.

So far as pityriasis rosea is concerned, this eruption comes within the limit of variability of pityriasis rosea as I have seen it. Nothing can be judged from

the appearance of the lesion on the thumb, which may or may not, so far as appearance goes, be a primary lesion. I should say that there is at least a reasonable possibility that this condition is not syphilis.

DR. KETRON: If a diagnosis of syphilis is ruled out, the possibility of the condition being an eruption due to drugs should be considered. The man tells me that his thumb has been dressed with various preparations, some of which may have been capable of giving rise to general toxic manifestations.

DR. APPEL: In Boston, we recently had two interesting cases somewhat similar to this. I had a patient with a history of a lesion on the neck which had been operated on, presumably for a tumor; the lesion proved to be a simple inflammation of the lymphatic nodes of the neck. Shortly after the operation an eruption appeared, a scaly papular eruption like syphilis. A blood test was taken, but fortunately treatment was not started until the report came back, which was negative. That test was made by the state laboratory. Another test taken a few days later was also reported negative. This led to a consultation, and it was thought that the patient had an atypical psoriasis. The blood sent to another laboratory came back with the Wassermann, Kahn and Hinton tests all strongly positive. We also had a nurse in the institution who developed a sore on the thumb which was neglected for a time, and then brought to the attention of the skin department. The Wassermann test of the blood was negative the first time; when repeated a few days later it was positive. With these cases in mind, I feel more safe in expressing the opinion that the case under discussion is syphilis in spite of the negative blood test.

DR. SCHAMBERG: Apropos of the reference that has been made to the absence of cubital adenopathy, I may say that Dr. MacKee in my presence found a distinct enlargement of the epitrochlear gland on the right side, and the arm of the affected side was so tender as to preclude a thoroughly satisfactory examination.

DR. HOWARD FOX: I saw the patient for the first time two days ago, at which time the appearance of the eruption suggested a macular syphilid. On observing the lesion on the finger and the adenopathy and the sequence of events, I felt convinced that the eruption was syphilitic. It was therefore a surprise to learn later that the Wassermann test was negative. As Dr. Stokes has intimated, it now seems that there is a reasonable doubt as to the diagnosis. No dark-field examination was made, as the lesions on the finger had been present so long and had been treated with iodine. No antisyphilitic treatment has been given, and we have no intention of beginning such treatment until the diagnosis of syphilis is definitely established.

DR. MALONEY: In answer to Dr. Stokes' question, the dark-field examination was not done because when the man came to the clinic the thumb was covered with iodine. Two specimens of blood were sent to different laboratories. Dr. Sharlit made two tests on our specimen, the results of both of which were negative. In the same batch of Wassermann tests he had four positive cases, so in all probability there was no error in the Wassermann technic. The original sore started seven weeks before presentation, and the eruption developed three weeks later. When we first saw the patient, two days ago, we thought the epitrochlear gland on the affected side was enlarged and that there was adenopathy in other parts of the body.

DR. MCCARTHY: The thing in this case of especial interest is the negative Wassermann test in secondary syphilis, assuming that it is a case of syphilis. We assume that the secondary stage of syphilis should give positive Wassermann tests in 100 per cent. It is quite probable that in a small number of cases, the spirochetal antigenic dosage is so powerful that the antibody blood reaction does not appear until after several days or weeks, even with the presence of a secondary rash.

MYCOSIS FUNGOIDES. Presented by DR. TRAUB.

S. E. was presented at the December, 1929, meeting of the New York Dermatological Society.

DISCUSSION

DR. SCHAMBERG: This case is interesting because the patches strongly resemble psoriasis, and I understand this was the initial diagnosis made; but if one palpates them or looks sharply, one sees that the patches are definitely more infiltrated than one sees in psoriasis, and the ulcerated tumor on the abdomen is suggestive of mycosis fungoides; I would concur in this diagnosis, stating at the same time that it is a very unusual case.

DR. KETRON: I see no reason why this patient cannot have both psoriasis and mycosis fungoides. As far as I know, psoriasis offers no immunity to mycosis fungoides, and in the ordinary run of events one would certainly occasionally find both diseases in the same patient. Some of the lesions, particularly on the upper extremities and trunk, are clinically characteristic of psoriasis. Perhaps histologic study would clear up the question.

DR. HOWARD FOX: I merely wish to call attention to the case I reported of psoriasis of twenty-eight years' duration in which the type of lesions changed and a typical picture of mycosis fungoides was presented. The histologic diagnosis of mycosis fungoides was made at that time by Dr. Pollitzer. We had a discussion at the last meeting of the New York Dermatological Society as to whether in similar cases the psoriatic lesions underwent mutation or were lesions of mycosis fungoides from the start. It seemed to me an academic discussion which was difficult to settle.

DR. HIGHMAN: I think the facts in connection with the discussion are so old that we have forgotten them. If you turn to Kaposi's textbook, or Jarisch or Finger, or to the older writers—Cazenave, for instance—you will find that one of the most common prefungoid lesions is the psoriatic one. As Dr. Fox mentioned, the sequence is an academic matter; and as this patient has mycosis fungoides and the lesions suggest psoriasis, we have to accept this as a psoriasiform type of a prefungoid lesion in a case of mycosis fungoides.

DR. DOWNING: I have a patient who presented typical lesions of psoriasis from 1918 to one year ago, and who received the usual treatment for psoriasis. A year ago, definite infiltrated plaques appeared. One of them was removed and a biopsy was done. The report was mycosis fungoides. This patient, up to the present time, has presented no tumor formation. The diagnosis has been confirmed by most of the dermatologists of the New England Dermatological Society.

DR. APPEL: In 1924 we had a patient at the Boston City Hospital who was in the last stages of generalized and ulcerating form of mycosis fungoides. The patient was well known to all the dermatologists of the New England Society, where she was shown several times. She was treated for a number of years in Boston for psoriasis, perhaps antedating the mycosis development by six or eight years, before the diagnosis was changed to mycosis fungoides. When she died, the entire body was covered with lesions of mycosis fungoides in various stages.

DR. FRASER: I am inclined to favor the views of Dr. Highman. We speak of psoriasiform lesions in syphilis which we know are not psoriasis, and I think it is proper to diagnose this case as a psoriasiform type of mycosis fungoides. It has been suggested that it is possible for the two conditions to exist in the same person at the same time. That is possible, but how are we going to prove it? Certainly not by the histology, for early prefungoid lesions can give a histologic picture indistinguishable from psoriasis. I brought out this point in an article published in 1917. I feel that we are not justified in concluding that this is mycosis fungoides incorporated on psoriasis. I believe that it was mycosis fungoides from the beginning.

CUTANEOUS SUPPURATION. Presented by DR. HIGHMAN.

The patient presented a universal eruption of about six years' duration, and he had been presented three years previously by Dr. Cummings at the Boston Meeting of the Atlantic Conference. The treatment had consisted of an incision and drainage of the abscesses, resection of the skin of the perineum, a Minot diet, transfusions, local antisepsis, diet, etc.

The laboratory work, which was extensive, gave mostly negative results; only staphylococci were found in the pus; there was a marked secondary anemia, and a slight hematuria. The patient has gained between 20 and 25 pounds (9 and 11.3 Kg.) and is practically cured.

DISCUSSION

DR. LORETTA J. CUMMINGS: I had the patient in my service at the Massachusetts General Hospital for a few months, and we were baffled by the condition. He came to New York to see Dr. Highman, who has done wonders for him. I am very glad to have this opportunity to congratulate Dr. Highman on the splendid work he has done in this case.

DR. KETRON: I should like to say a word with reference to the importance of very thorough and repeated bacteriologic investigation in cases of this character, without casting any reflections, however, on the work which has been done in the present case. To illustrate: We recently saw a patient at the Johns Hopkins Hospital who had been suffering for a considerable time with multiple abscesses affecting the upper portion of the back. He was sent into the hospital, where bacteriologic examination and animal inoculation were carried out with essentially negative results. The patient was discharged, but later on was readmitted into the hospital. At this time a large piece of tissue was excised, cultures from which showed an anaerobic actinomyces which is believed to be the cause of the disease.

It seems to be common with many of us that the extent of cultures taken from obscure cases consists in inoculating with pus a few tubes of Sabouraud's medium and perhaps some broth or agar plates. It is quite probable that the pus frequently does not contain viable organisms, and repeated cultures from various lesions may be necessary to demonstrate the organism or perhaps, as in the case just noted, it may be necessary to cultivate some of the infected tissues in various ways. I believe that we have hardly scratched the surface in our discoveries of fungus infections, and extensive bacteriologic studies may reveal in the future many new mycoses of which we have no knowledge at the present time.

DR. DOWNING: I should like to ask Dr. Highman what the successful treatment was that he used in this case.

DR. WEIDMAN: I should like to know something about the bacteriologic examination.

DR. HIGHMAN: If I were to tell all that was done and all the work that was required, it would make a monograph. The laboratory investigations included anaerobic and aerobic cultures, and guinea-pigs were put to a terrific strain to maintain the vital statistics. We found an anaerobic streptococcus just once, but it could not be done again. Save this, no bacteria, fungi or protozoa were discovered other than the staphylococcus. Other clinical pathologic work was done routinely and the boy was found to have a severe secondary anemia. Here was a boy with abscesses, pyoderma if you will, in which we found only staphylococcus. The treatment was mainly surgical procedure, and the fact that the boy is as well as he is, is due to the surgical work of Dr. Moschowitz, who has devoted much time to the case, carrying out excision and drainage and ablations of undermined lesions when these had to be done. The perineum and buttocks were a mass of lesions requiring total resection of the skin in that vicinity. The general medical treatment consisted of tonics and diet. This was a year and a half before Sutton's publication of the use of the Minot diet in skin suppuration, but it seems to me that the real problem was the curious lack of resistance to the staphylococcus,

which might be altered by transfusions. Nothing else is known to me which so raises resistance; therefore, I though I would try this. The improvement involves no esthetic perfection, but the boy is practically well, is driving his car, and leading a normal existence.

BASAL CELL EPITHELIOMA WITH METASTASES. Presented by DR. ELLER.

T. E. was previously presented at the Manhattan Dermatological Society in October, 1928. Tissue from the original lesion on the finger, and later from lesions on the forearm and an axillary node, all showed the basal cell type of epithelioma.

DISCUSSION

DR. HAZEN: Basal cell cancer of the limbs is unsual; the squamous cell type is much more common. In the second place, true basal cell tumors of the type described by Krompecher very rarely metastasize. In a study of over 800 cases in Bloodgood's pathologic laboratory, there was but a solitary case in which a basal cell growth had spread to the lymph nodes. However, a cuboid cell growth may readily be mistaken for a basal cell growth and yet will metastasize at a late period, or a mixed growth may occur in which the squamous cells eventually break through.

DR. FRASER: I agree with Dr. Hazen. Metastases from the ordinary type of basal cell epithelioma which arises in the hair matrix is rare or does not occur. I am convinced that this is a sweat duct cancer. I do not believe that the side shown here is from an axillary node. When a lymph node is infiltrated with cancer cells, there are usually some remnants of lymphoid structure left. I agree with Dr. Eller that the tumor is of the basal cell type which arises from a sweat duct epithelium.

DR. WEIDMAN: I saw the section and agree that this is a sweat duct carcinoma. The characteristics are not merely those of a Krompecher affair; there are whorling tendencies in some of the nests that do not nearly amount to pearls, but are still sufficient to indicate pearly traits, and this in turn, a prickle cell nature. Furthermore, normal sweat ducts show the squamous type of cell in the luminal layer (we may even see a thin hyaloid line immediately around the lumen, which is the homologue of the stratum corneum of the surface, which brings the squamous theme further into line in this case. There is, altogether, not much difficulty in alining the clinical malignancy in this case with our preconceived notions of the histologic criteria in the subject.

As to the specimen from the axilla, I did not recognize any adenoid tissue there either; of course, where we have very large carcinomatous nodes, say the size of a goose egg, it would still be quite possible to have a block submitted for study which would be entirely carcinomatous; but, even at that, the architecture in the node is consistent with that in the skin; more like that of the squamous cell cancer—in large circular masses.

DR. FRASER: I agree with Dr. Weidman that it is possible but not probable. I cannot recall examining a specimen where there was not some evidence of lymphatic tissue.

A CASE FOR DIAGNOSIS (PLASMA-CELL TUMOR). Presented by DR. MACKEE.

I. S., a girl, aged 14, born in the United States, was first seen at the Post-Graduate Skin Clinic on Aug. 22, 1929. On the dorsum of the right hand, in the region of the third metacarpophalangeal joint, there was a firm, oval, sharply defined, scaly, violaceous-red lesion about 1 by 2.5 cm. in size. Proximal to this were several other scaly, slightly elevated lesions about the size of a small pea. All these legions were distinctly infiltrated. On the palmar surface of the middle finger were numerous ill defined scaly lichenoid papules the size of a pinhead. The patient was uncertain of the duration, but thought that the eruption appeared

when she was a baby. Examination for fungi was negative. The Wassermann test was negative.

A pathologic report by Dr. Satenstein showed that there was a dense cellular infiltration extending from the epidermis down to the mid cutis. This was most marked in the center of the section, and tapered off toward the edge. Scattered throughout the cellular mass were very many small vessels. The vessels of the subpapillary zone were dilated and some contained fibrin and red blood cells. The epidermis was irregularly acanthotic. The cells were practically all plasma cells. Ewing, in his book, "Neoplastic Diseases," in the chapter on lymphoma and lymphosarcoma and under the heading of "Extra-medullary Plasma Cell Tumors," called attention to a similar condition. The possibility of a plasma cell sarcoma or of a nevus is suggested. We have a specimen from another case of a nevoid lesion which was entirely composed of the embryonic type of plasma cell, similar to that seen about vessels in granulation tissue.

MULTIPLE EPITHELIOMATOSES CUTIS (GRENZ RAY TREATMENT). Presented by DR. ELLER.

A man, from the Post-Graduate Skin Clinic, presented lesions on the trunk, neck and upper extremities, the condition having existed for fifteen years. The lesions began as flat, scaly, erythematous plaques about the size of a pea, and enlarged by peripheral extension. The lesions had all been treated with erythema doses of Grenz rays and were rapidly undergoing involution. Biopsy revealed basal cell epithelioma.

On March 15, 1928, the patient was admitted to the hospital for the third time, and showed several hard, adherent, immovable masses in the right axilla, with marked edema of the arm and forearm. Histologic examination of the axillary glands showed typical metastatic squamous cell carcinoma. He was then referred to the Memorial Hospital, where a complete shoulder girdle amputation was done. A roentgenogram of the chest, taken just before the amputation, was negative. The patient did quite well after this, gained 12 pounds (5.4 Kg.) in weight, and showed no evidence of further metastases until February, 1929, when a metastatic node appeared in the supraclavicular fossa. This was also excised. Dr. Ewing reported the tissue removed as an "epidermoid carcinoma." No further recurrences had appeared. The patient's general health had been excellent.

POSSIBLE AVIAN TUBERCULOSIS WITH SKIN LESIONS. Presented by DR. RULISON.

F. T., a woman, a book-keeper, aged 26, born in the United States, presented lesions on the right side of the scalp, on the right malar eminence, both ears, the nose, lower lip and hard palate. At the age of 16, she had had enlargement of the right cervical glands, which was diagnosed as tuberculous adenitis. She was given ten roentgen treatments, and the adenopathy decreased, but the glands had remained palpable. Four years later, a younger sister had cervical adenitis, with drainage of the gland.

Five years previous to presentation, erythematous, scaly and crusting lesions appeared, first noted in the scalp and on the right side of the face. These lesions were slowly progressive, showed occasional improvement, but never entirely cleared up. Alopecia developed in the scalp lesion. Scarring was present. The nose showed erythema and crusting; the lips showed scaling and atrophy; the hard palate some ulcerations, and the ears showed erythema and scaling.

The patient had received considerable treatment for lupus erythematosus. Diseased teeth had been removed, and a tonsillectomy performed. Roentgen examinations of the nasal accessory sinuses and the thorax were negative. The patient was given sixty-four injections of a gold compound, with no improvement.

She was first seen at the Cornell Clinic on Nov. 15, 1929. Her weight at that time was 110 pounds (49.9 Kg.). A physical examination gave negative results,

except for a slight spinal curvature. Roentgen examination of the thorax, abdomen and hips was negative except for the probable presence of calcified mesenteric lymph nodes. The blood count was: polymorphonuclears, 60 per cent; lymphocytes, 39 per cent; eosinophils, 1 per cent. The intradermal avian tuberculin test was four plus. The Pirquet tests was as follows: bovine, plus-minus; human, one plus.

Two biopsies were taken from the scalp lesions (microscopic section exhibited), and scrapings were taken from the nose; catheterized specimen of the urine was obtained, and the right cervical gland was removed. A careful search was made for tubercle bacilli in these specimens, but without success, except in the cervical gland, where tubercle bacilli were demonstrated. Laboratory animals and birds were inoculated, but insufficient time had elapsed for report on these inoculations. Various culture mediums had been smeared and incubated.

DISCUSSION

DR. SCHAMBERG: Clinically, I believe that this is a typical case of lupus erythematosus; but there are other features brought out by the examinations made which throw some doubt on that diagnosis. I understand that tubercle bacilli were found in the lympathic glands and that a local cutaneous test suggested the possibility of avian tuberculosis. Avian tuberculosis in man is a dangerous and sometimes a fatal condition. I saw a case in Vienna, shown to me by Dr. Urbach: this patient ran a fever and had certain cutaneous and mucous membrane lesions. By proper laboratory study, particularly the differential susceptibility of mammals and birds, the nature of the lesions may be determined.

DR. RULISON: So far as I know, there is no case of avian tuberculosis with skin lesions in the American literature. This case was first seen on November 15, so that not enough time has elapsed to prove the diagnosis by cultural growth and animal inoculation. However, the avian tuberculin reaction is so specific, and the response in this case was so intense, that there is reason to hope that the avian bacillus may be isolated. The patient will be treated with avian tuberculin, and a cure is possible.

There are in the literature four cases of avian skin tuberculosis which have been cured by avian tuberculin. Also, Urbach's case of avian skin tuberculosis showed improvement under this treatment. The patient in the case presented says that the tuberculin diagnostic test made three weeks ago has been followed by more improvement than she has ever had.

As Dr. Schamberg pointed out, the skin lesions look like lupus erythematosus and they have been so diagnosed at two skin clinics in this city. Such a diagnosis is not inconsistent with the finding of the avian bacillus as its cause, for lupus erythematosus may arise from a number of different toxic agents. However, the case is atypical in that they are ulcerations of the mucous membrane of the hard palate, the scaling is atypical, the crusting all along the bridge of the nose is unusual, and the condition has resisted the removal of all the discoverable foci of infection and the administration of seventy-nine doses of gold and sodium thiosulphate during two years. Lipschutz, Urbach, Volk, and Nicolau and Blumenthal have reported the four cases of avian tuberculosis of the skin to be found in the literature.

UNUSUALLY EXTENSIVE NEVUS FLAMMEUS OF UNILATERAL DISTRIBUTION. Presented by DR. BECHET.

E. S., a woman, aged 27, had had since birth, a bright red port wine mark covering the entire left half of the face, with a perfectly sharp line of demarcation on the upper lip, chin and within the mouth and pharynx. The lesion also involved the entire left arm and upper left side of the trunk; the leg also was involved.

A Case for Diagnosis (Syphilis?). Presented by Dr. MacKee.

Y. L., had been presented at the March, 1929, meeting of the Dermatological Section of the Academy of Medicine. The diagnosis at that time was tertiary syphilis, and the histology resembled a tertiary syphilis. The Wassermann reaction was negative and continued to be so. The patient was given antisyphilitic treatment consisting of twenty-four injections of bismuth and ten injections of neoarsphenamine. The lesions slowly disappeared. However, during the month previous to the second presentation, there appeared three or four patches under the right eye and on the right side of the nose, about the size of a split pea and resembling lupus erythematosus.

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Directory of Dermatologic Societies *

NATIONAL DERMATOLOGIC SOCIETIES

American Medical Association, Scientific Assembly, Section on Dermatology and Syphilology

William H. Guy, Chairman, Jenkins Arcade, Pittsburgh.
Francis E. Senear, Secretary, 55 E. Washington St., Chicago.
Place: Detroit. Time: June 23-27, 1930.

American Dermatological Association

Udo J. Wile, President, University Hospital, Ann Arbor, Mich.
C. Guy Lane, Secretary, 416 Marlborough St., Boston.
Place: Cleveland. Time: June 19-21, 1930.

British Association of Dermatology and Syphilology (Canadian Branch)

Gustave Archambault, President, 544 East Sherbrooke, St., Montreal.
Albéric Marin, Secretary, 544 East Sherbrooke St., Montreal.
Place: Montreal. Time: June, 1930.

SECTIONAL DERMATOLOGIC SOCIETIES

Baltimore and Washington Dermatological Society

Frank J. Eichenlaub, President, 1835 I St., N. W., Washington, D. C.
Leon Ginsburg, Secretary, 1800 N. Charles St., Baltimore.

Iowa and Western Illinois Dermatological Association

Robert E. Jameson, President, 1015 First National Bank Bldg., Davenport, Iowa.
A. T. Leipold, Secretary, 1419½ 5th Ave., Moline, Ill.

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Thomas A. Maxwell, Secretary-Treasurer, 1119 Union Indemnity Bldg., New Orleans.

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Albert R. McFarland, Secretary, 348 University Ave., Rochester.

* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

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